

# The interplay of global standards and EU pharmaceutical regulation

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**The Interplay of Global Standards and  
EU Pharmaceutical Regulation**

**The Interplay of Global Standards and  
EU Pharmaceutical Regulation**

*Sabrina Röttger-Wirtz*

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**The Interplay of Global Standards and  
EU Pharmaceutical Regulation**

DISSERTATION

to obtain the degree of Doctor  
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Prof. dr. Rianne M. Letschert  
in accordance with the decision of the Board of Deans,  
to be defended in public  
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## List of Abbreviations

|            |   |
|------------|---|
| AIDS       | Acquired Immune Deficiency Syndrome   |
| ANVISA     | Agência Nacional de Vigilância Sanitária (Brazil)                                     |
| APEC       | Asia-Pacific Economic Cooperation   |
| APIC       | Active Pharmaceutical Ingredients Committee   |
| ASEAN      | Association of Southeast Asian Nations  |
| AVBWasserV | Regulation on General Conditions for Water Supply                                     |
| Bfarm      | German Federal Institute for Drugs and Medical Devices                                |
| BIO        | Biotechnology Innovation Organisation   |
| BSE        | Bovine Spongiform Encephalopathy  |
| CARR       | Centre for Analysis of Risk and Regulation  |
| CAT        | Committee for Advance Therapies   |
| CEN        | European Committee for Standardisation  |
| Cenelec    | European Committee for Electrotechnical Standardisation                               |
| CDSO       | Central Drugs Standard Control Organization (India)                                   |
| CECMED     | Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos (Cuba) |
| CFDA       | Chinese Food and Drug Administration  |
| CHMP       | Committee for Medicinal Products for Human Use  |
| CIOMS      | Council for International Organizations of Medical Sciences                           |
| CMDh       | Coordination Group for Mutual Recognition and Decentralized Procedures                |
| COFEPRIS   | Comisión Federal para la Protección contra Riesgos Sanitarios (Mexico)                |
| COMP       | Committee for Orphan Medicinal Products   |
| COSS       | Committee on Safe Seas and the Prevention of Pollution from Ships                     |
| CPMP       | Committee for Proprietary Medicinal Products  |
| CTD        | Common Technical Document   |
| CVMP       | Committee for Medicinal Products for Veterinary Use                                   |
| DG SANTE   | Directorate General for Health and Food Safety  |
| DIN        | Deutsches Institut für Normung  |
| DoHs       | Departments of Health   |
| DRAs       | Drug Regulatory Authorities   |
| DVGW       | Deutsche Vereinigung des Gas- und Wasserfaches  |
| EAC        | East African Community  |
| EC         | European Commission   |
| ECHA       | European Chemicals Agency   |
| eCTD       | electronic version of the Common Technical Document                                   |
| EDQM       | European Directorate for the Quality of Medicines & HealthCare                        |
| EEA        | European Economic Area  |
| EEC        | European Economic Community   |
| EFPIA      | European Federation of Pharmaceutical Industries and Associations                     |
| EFSA       | European Food Safety Authority  |
| EFTA       | European Free Trade Association   |
| EMA        | European Medicines Agency   |
| ENVI       | Environment, Public Health and Food Safety  |

LIST OF ABBREVIATIONS

|               |   |
|---------------|---|
| EPPO          | European and Mediterranean Plant Protection Organisation  |
| ERTA          | European Road Transport Agreement   |
| ESTI          | European Telecommunications Standards Institute   |
| EU            | European Union  |
| Eurocontrol   | European Organisation for the Safety of Air Navigation  |
| EWG           | Expert Working Group  |
| FAO           | Food and Agriculture Organisation   |
| FDA           | Food and Drug Administration  |
| GAL           | Global Administrative Law   |
| GATT          | General Agreement on Tariffs and Trade  |
| GAVI Alliance | Global Alliance for Vaccine Immunization  |
| GCP           | Global Cooperation Group  |
| GHC           | Gulf Health Council   |
| GHS           | Globally Harmonised System  |
| Global GAP    | Global Good Agricultural Practices  |
| GMP           | Good Manufacturing Practice   |
| GSA           | Ghana Standards Authority   |
| HAS           | Health Sciences Authority (Singapore)   |
| HCPWP         | Healthcare Professionals Working Party  |
| HMPC          | Committee on Herbal Medicinal Products  |
| HPFB          | Health Products and Food Branch   |
| ICAO          | International Civil Aviation Organisation   |
| ICH           | International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use |
| ICJ           | International Court of Justice  |
| IFPMA         | International Federation of Pharmaceutical Manufacturers Associations   |
| IGBA          | International Generic and Biosimilar Medicines Association  |
| IGPA          | International Generic Pharmaceutical Alliance   |
| ILO           | International Labour Organisation   |
| IMO           | International Maritime Organisation   |
| INGO          | International Non-governmental Organisation   |
| IO            | International Organisation  |
| IPEC          | International Pharmaceutical Excipient Council  |
| IPPC          | International Plant Protection Convention   |
| IPRF          | International Pharmaceutical Regulators Forum   |
| ISO           | International Organisation for Standardisation  |
| IWG           | Implementation Working Group  |
| JEFCA         | Joint FAO/WHO Expert Committee on Food Additives  |
| JPMA          | Japan Pharmaceutical Manufacturers Association  |
| KOWSMD        | Public Authority for Industry Standards and Industrial Services Affairs (Kuwait)  |
| LIBNOR        | Lebanese Standards Institution  |
| MCC           | Medicines Control Council (South Africa)  |
| MedDRA        | Medical Dictionary for Regulatory Activity  |
| MFDS          | Ministry of Food and Drug Safety (South Korea)  |
| MHW           | Ministry of Health and Welfare in Japan   |
| MHLW          | Ministry of Health, Labour and Welfare  |
| MSSO          | Maintenance and Support Services Organisation   |

|                 |  |
|-----------------|--|
| National Center | National Center for the Expertise of Drugs, Medical Devices and Equipment (Kazakhstan) |
| NGO             | Non-Governmental Organisation  |
| NTA             | Notice to Applicants   |
| OECD            | Organisation for Economic Co-operation and Development                                 |
| OIE             | World Organisation for Animal Health   |
| OIV             | International Organisation of Vine and Wine  |
| OJ              | Official Journal   |
| PANDRH          | Pan American Network for Drug Regulatory Harmonization                                 |
| PDCO            | Paediatric Committee   |
| PhRMA           | Pharmaceutical Research and Manufacturers of America                                   |
| PIC/S           | Pharmaceutical Inspection Co-operation Scheme  |
| PMDA            | Pharmaceuticals and Medical Devices Agency   |
| PPP             | Public-Private Partnership   |
| PRAC            | Pharmacovigilance Risk Assessment Committee  |
| PWCP            | Patients' and Consumers' Working Party   |
| Q&A             | Questions & Answers  |
| RAAPAC          | Regulatory Acceptance of Analytical Procedures and/or Acceptance Criteria              |
| REACH           | Registration, Evaluation, Authorisation and Restriction of Chemicals                   |
| ReNEUAL         | Research Network on European Administrative Law  |
| RHI             | Regional Harmonisation Initiatives   |
| SADC            | Southern African Development Community   |
| SOP             | Standard Operating Procedure   |
| SPS             | Sanitary and Phytosanitary Agreement   |
| TBT             | Technical Barriers to Trade  |
| TEU             | Treaty on European Union   |
| TFDA            | The Food and Drug Administration (Chinese Taipei)                                      |
| TFEU            | Treaty on the Functioning of the European Union  |
| TGA             | Therapeutic Goods Administration (Australia)   |
| UN              | United Nations   |
| UNESCO          | United Nations Educational, Scientific and Cultural Organisation                       |
| US/USA          | United States (of America)   |
| USP             | United States Pharmacopeia   |
| WADA            | World Anti Doping Agency   |
| WHO             | World Health Organisation  |
| WSMI            | World Self-Medication Industry   |
| WTP             | World Trade Organisation   |
| WWF             | World Wildlife Fund  |



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## Introduction

### 1. EU PHARMACEUTICAL REGULATION IN THE AGE OF GLOBALISATION

The regulation of pharmaceuticals in the European Union (EU), like many other regulatory areas, has attracted critical attention. Public trust in the regulation of pharmaceuticals has been shaken by incidents such as the ‘Mediator Scandal’: the diabetes medication Benfluorex, sold by Servier in France under the name Mediator, was withdrawn from the French market in 2009.<sup>1</sup> The European Medicines Agency recommended in December 2009 that all drugs containing Benfluorex be withdrawn from the European market.<sup>2</sup> These steps had to be taken because it was revealed that the drug causes heart disease, and led to between 500 and 2,000 deaths in the 30 years it has been available.<sup>3</sup> Also the marketing authorisation of anti-diabetes drug Avandia, sold by GlaxoSmithKline, was suspended,<sup>4</sup> causing a scandal which affected public trust regulators.<sup>5</sup>

These incidents show how complex and challenging it is to authorise the marketing of a medicinal product. In the field of pharmaceuticals, scientific and technical progress has benefited humanity in enhancing the quality of life and life expectancy. Pharmaceuticals are heavily regulated products and extensive standard-setting takes place on national, European and global levels. From a risk regulation perspective pharmaceutical standards are a stimulating field of research, as potent drugs usually come with side effects, posing a risk to human health. Although these side effects are accepted for the benefits these products offer, there is still a decision to be made on whether or not the benefits outweigh the costs of a medical product. A marketing authorisation requires a choice of high expertise.<sup>6</sup> However, as with other risk regulation measures, there are also significant uncertainties at the time a medicinal product is authorised – not all risks can be determined by tests carried out before a marketing authorisation is granted.<sup>7</sup>

The EU has a long record of tragedies with various consumer products threatening human health. This is exemplified by bovine spongiform encephalopathy (BSE), the dioxin

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<sup>1</sup> A. Mullard, ‘Mediator Scandal Rocks French Medical Community’, 377(9679) *The Lancet* (2011), pp. 890-892.

<sup>2</sup> EMA, Press Release – European Medicines Agency recommends withdrawal of benfluorex from the market in the European Union, EMA/CHMP/815033/2009, 18 December 2009, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Press\\_release/2010/01/WC500059714.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/01/WC500059714.pdf), last accessed: 3 April 2017.

<sup>3</sup> Mullard (2011), p. 890.

<sup>4</sup> EMA, Press Release – European Medicines Agency recommends suspension of Avandia, Avandamet and Avaglim, EMA/585784/2010, 23 September 2010, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Press\\_release/2010/09/WC500096996.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/09/WC500096996.pdf), last accessed: 3 April 2017; C. Briseño, ‘Skandal-Medikament Avandia: Diabetes-Blockbuster droht das Aus, Der Spiegel, 07.09.2010; available via: <http://www.spiegel.de/wissenschaft/medizin/skandal-medikament-avandia-diabetes-blockbuster-droht-das-aus-a-715917.html>, last accessed: 3 April 2017.

<sup>5</sup> F. Boudier, ‘Handling Pharmaceutical Risks in Post-Trust Society – Science-based decision making under strain?’, in M. van Asselt, M. Everson & E. Vos (Eds.), *Trade, Health and the Environment – The European Union Put to the Test* (Oxon & New York: Routledge/Earthscan, 2014), pp. 91-112, p. 94.

<sup>6</sup> H. Eichler, B. Bloechel-Daum, D. Brasseur, A. Breckenridge, H. Leufkens, J. Raine, T. Salmonson, C. Schneider & G. Rasi, ‘The Risks of Risk Aversion in Drug Regulation’, 12(12) *Nature Reviews Drug Discovery* (2013), pp. 907-916.

<sup>7</sup> Eichler, Bloechel-Daum, Brasseur, Breckenridge, Leufkens, Raine, Salmonson, Schneider & Rasi (2013), p. 907.

contamination of food produced in Belgium, foot and mouth-disease, and contaminated blood in France, to name but a few.<sup>8</sup> In response to these events, the EU developed an extensive regulatory framework on goods and the risks associated with them. Reactions to risks are what constitute the largest source of regulation of the EU internal market.<sup>9</sup> It requires the EU legislature to strike a delicate balance between two Treaty goals: the internal market with free movement of goods on the one hand, and protecting public health, the environment and consumers on the other hand.<sup>10</sup>

In this regard, risk regulation is not limited to legally-binding legislative and non-legislative measures, but also encompasses health, safety and quality standards for products and production processes.<sup>11</sup> Such regulatory standards form the object of this research. They are voluntary, measurable criteria governing certain technical and/or scientific matters of a product or production process.<sup>12</sup> These types of measures are not given much attention in legal research due to their technical or scientific nature and non-binding form.<sup>13</sup> However, they are deeply intertwined with the legal frameworks of risk regulation, as this research will show with regard to the regulation of pharmaceuticals.

At the same time, risk regulation increasingly evolves into an exercise carried out at multiple levels – national, European and international – creating complicated and often interconnected structures of regulatory organisations and procedures.<sup>14</sup> Standard-setting on the global level facilitates the free trade of products. Moreover, it brings together expertise from all over the world which benefits the quality of the standards set.<sup>15</sup> The process of globalisation through the growing interrelation of markets, communication and traffic structures,<sup>16</sup> led to ‘de-territorialised’<sup>17</sup> regulation in the form of global regulatory standards.

<sup>8</sup> See: D. Vogel, ‘The New Politics of Risk Regulation in Europe’, CARR Discussion Papers, DP 3, Centre for Analysis of Risk and Regulation, London School of Economics and Political Science, (2001).

<sup>9</sup> A. Alemanno, ‘The Shaping of European Risk Regulation by Community Courts’, Jean Monnet Working Paper 18/2008, (2008), p. 4.

<sup>10</sup> A. Alemanno, ‘Regulating the European Risk Society’, in A. Alemanno, F. den Butter, A. Nijssen & J. Torriti (Eds.), *Better Business Regulation in a Risk Society* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. 37-56, p. 40.

<sup>11</sup> C. Scott, ‘Standard-Setting in Regulatory Regimes’, in R. Baldwin, M. Cave & M. Lodge (Eds.), *The Oxford Handbook of Regulation* (Oxford: Oxford University Press, 2010), pp. 104-119.

<sup>12</sup> The definition of global standards will be discussed in Chapter 1, Section 2.2.

<sup>13</sup> Some notable exceptions are: B. Dorbeck-Jung, ‘Challenges to the Legitimacy of International Regulation: The Case of Pharmaceuticals Standardisation’, in A. Føllesdal, R.A. Wessel & J. Wouters (Eds.), *Multilevel Regulation and the EU: The Interplay between Global, European and National Normative Processes* (Leiden/Boston: Martinus Nijhoff Publishers, 2008), pp. 51-71; N. Hachez & J. Wouters, ‘A Glimpse at the Democratic Legitimacy of Private Standards: Assessing the Public Accountability of Global G.A.P.’, 14(3) *Journal of International Economic Law* (2011), pp. 677-710; H. Röhl, ‘Internationale Standardsetzung’, in C. Möllers, A. Vosskuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 319-343.

<sup>14</sup> J. Habermas, ‘Die Postnationale Konstellation und die Zukunft der Demokratie’, in J. Habermas, *Die Postnationale Konstellation – Politische Essays* (Frankfurt am Main: Suhrkamp Verlag, 1998), pp. 91-169, p. 165.

<sup>15</sup> K. Abbott & D. Snidal, ‘International ‘standards’ and international governance’, 8(3) *Journal of European Public Policy* (2001), pp. 345-370, p. 366.

<sup>16</sup> Habermas (1998), p. 101.

<sup>17</sup> For the notion of de-territorialisation (‘Entterritorialisierung’ in German) see: Vereinigung der Deutschen Staatsrechtslehrer, ‘Entterritorialisierung des Öffentlichen Rechts’, 76 *Veröffentlichungen der Vereinigung der Deutschen Staatsrechtslehrer* (2017), pp. 245-443; H. Hofmann, ‘Dealing with Trans-Territorial Executive Rule-Making’, 78(3) *Missouri Law Review* (2013), pp.

This challenges the classical perception of regulators operating in a national administration, with powers confined to a single state.<sup>18</sup> The reason for the globalisation of regulation cannot only be found in the proliferation of global trade, but also in the nature of the risks faced by society today which become increasingly complex as the causes and factors that influence them are increasingly interconnected and interdependent, going far beyond national borders and areas of competence.<sup>19</sup> Efficient risk regulation is no longer feasible through purely national measures. Therefore, global standards implemented in the EU increasingly shape the regulation of risk in the Union. At the same time, the EU also shapes regulatory rules on a global level.<sup>20</sup>

It is increasingly acknowledged in the literature that standards developed on a global level influence policies and decisions in the European Union.<sup>21</sup> What is lacking is an analysis of their implementation and an assessment of the influence these standards have on risk regulation in the EU. Nonetheless, an in-depth understanding of the impact of these standards on EU risk regulation is essential to fully evaluate the role of global standards. It is imperative to clarify the interaction of regulators at the global level and the ramifications of the standards they set for the framework that constitutes EU risk regulation. Since global standards are developed by a large variety of bodies and in a wide array of regulatory fields, a complete analysis of the phenomenon is not within the scope of this PhD research. Hence, the focus here is on in-depth research of the institutional structure, decision-making process of global standards, and their impact on the EU risk regulation framework in the regulation of pharmaceuticals.

What makes this field especially relevant for an in-depth study of global standards is the balance between industrial interests and public health concerns which are inherent in this field. Like risk regulation in general, pharmaceutical regulation needs to balance protection of the public good, in this case public health, with the industrial interests of marketing a specific product, which has risks attached to it. Three policy areas collide in the regulation of medicines: the protection of public health, policies regarding the healthcare system, and industrial policy.<sup>22</sup>

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423-442, p. 426; C. Tietje, *Internationalisiertes Verwaltungshandeln* (Berlin: Duncker & Humblot GmbH, 2001), p. 173; K. Ladeur, 'Die Internationalisierung des Verwaltungsrechts: Versuch einer Synthese', in C. Möllers, A. Vosskuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 375-394, p. 376 and 394.

<sup>18</sup> C. Harlow, 'Composite Decision-Making and Accountability Networks: Some Deductions from a Saga', 32(1) *Yearbook of European Law* (2013), pp. 3-29, p. 3.

<sup>19</sup> J. Black, 'Critical Reflections on Regulation', Centre for Analysis of Risk and Regulation, CARR Discussion Papers DP 4 (2002), London School of Economics and Political Science, London, UK, p. 3; Habermas (1998), pp. 91-169.

<sup>20</sup> See in this regard especially the recent work of Joanne Scott: J. Scott, 'The New EU "Extraterritoriality"', 51(5) *Common Market Law Review* (2014), pp. 1343-1380; J. Scott, 'Extraterritoriality and Territorial Extension in EU Law', 62(1) *American Journal of Comparative Law* (2014b), pp. 87-125.

<sup>21</sup> See e.g. J. Wouters & S. Verhoeven, 'Regulation and Globalization: Interaction between International Standard-setting Agencies and the European Union', in D. Geradin, R. Muñoz & N. Petit (Eds.), *Regulation Through Agencies in the EU: A New Paradigm of European Governance* (Cheltenham: Edward Elgar, 2006), pp. 256-273; J. Mendes, 'Rule of Law and Participation: A Normative Analysis of Internationalized Rulemaking as Composite Procedures', 12(2) *International Journal of Constitutional Law* (2014), pp. 370-401; Röhl (2007), pp. 319-343; P. Müller-Graff, 'Das "Soft Law" der Europäischen Organisationen', 1 *Europarecht* (2012), pp. 18-34.

<sup>22</sup> G. Permanand, *EU Pharmaceutical Regulation: The Politics of Policy-Making* (Manchester: Manchester University Press, 2006), p. 4.

Thus, the patient's interest in obtaining safe medicines that effectively cure or treat a certain illness have to be balanced with the industry interest in obtaining marketing authorisations for their products and to keep the research and development phase as cost-effective as possible. Pharmaceuticals regulation needs to take the at times conflicting interests of patients, doctors, pharmacists, as well as the pharmaceutical industry, into consideration.<sup>23</sup> Where such a multitude of interests have to be balanced in regulatory decisions and the standards set are of a protective nature, a careful analysis of how global pharmaceutical standards influence the EU pharmaceutical regulatory system becomes imperative. Therefore, the underlying question to be addressed in this research is:

What legal challenges arise from the interplay of global standards and EU pharmaceutical regulation?

In order to address this question, the research will study the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) closely. Before 2015 the ICH was known as the International 'Conference on' Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use. The ICH is a global standard-setting body consisting of both representatives of regulatory authorities as well as of pharmaceutical industry associations. It has been selected as it has established itself as the main standard-setting body in the field of pharmaceuticals.

## 2. GLOBAL STANDARD-SETTING: RAISING QUESTIONS OF LEGITIMACY

The increasing relevance of global standards poses a challenge to the traditional structure of administrative action from an institutional, substantive and procedural perspective, for the regulatory systems implementing them. Furthermore, risk regulation through global standards does not fit easily into the state-centred perspective traditional international law takes. The mechanisms and actors involved in this form of regulation challenge a narrow definition through traditional international law.<sup>24</sup> This is exemplified with regard to the ICH, a public-private body where regulators and private interest representatives work together towards common standards. The integration of private actors in regulatory bodies is driven by the knowledge provided by regulated industry,<sup>25</sup> yet also opens the regulatory process up to the danger of regulatory capture.<sup>26</sup>

Global regulatory initiatives have been criticised for taking place in a rather technocratic and closed setting, by regulators and representatives of the industry hiding from public scrutiny.<sup>27</sup> Although global cooperation in standard-setting seems to be an imperative

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<sup>23</sup> E. Mossialos, M. Mrazek & T. Walley, 'Regulating Pharmaceuticals in Europe: An Overview?', in E. Mossialos, E. Mrazek & T. Walley (Eds.), *Regulating Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality* (Maidenhead: Open University Press, 2004), pp. 1-37, p. 5.

<sup>24</sup> See also: Black (2002).

<sup>25</sup> Abbott & Snidal (2001), p. 355.

<sup>26</sup> For further literature on regulatory capture see: G. Stigler, 'The Theory of Economic Regulation', 2(1) *The Bell Journal of Economics and Management Science* (1971), pp. 3-21; T. Makkai & J. Braithwaite, 'In and Out the Revolving Door: Making Sense of Regulatory Capture', 12(1) *Journal of Public Policy* (1992), pp. 61-78.

<sup>27</sup> See e.g.: A. Føllesdal, R. Wessel & J. Wouters (Eds.), *Multilevel Regulation and the EU: The Interplay between Global, European and National Normative Processes* (Leiden: Koninklijke Brill, 2008); A. Slaughter, 'The Accountability of Government Networks', 8(2) *Indiana Journal of Global Legal*

response to complex risks faced today, its legitimacy has been criticised. For example, Shapiro claims that in transnational governance ‘decision-making processes are relatively new and tend to be elitist and opaque, with few participants and no agreed upon control’.<sup>28</sup> Problems that have been highlighted include a lack of consumer interest or civil society participation in global standard-setting. This points to the failure of establishing a system that represents the interests of society at large, and not just industrial interests.<sup>29</sup> Standard-setting in global bodies is often carried out through an informal process in the sense that it deviates from formalities related to the output, process and actors when compared to traditional international law.<sup>30</sup> In the context of global standard-setting, the regulated industry is an active player in the decision-making process, which has led authors to claim that while accountability towards the public at large is often lacking, these processes are mostly accountable to the regulated industry.<sup>31</sup>

These concerns also have been voiced with regard to the ICH, as the standard-setting process has been criticised for its lack of transparency,<sup>32</sup> and for making decisions in closed groups of experts, intertwining science with politics.<sup>33</sup> In the ICH’s practice, the pharmaceutical industry and regulatory authorities are to be regarded as privileged stakeholders in the international standard-setting of pharmaceuticals, while input from patient and doctor associations seems to be of lesser relevance.<sup>34</sup> Critics have even stated that ‘the ICH process has permitted scientists from industry to renegotiate extensively the scientific standards that the regulatory agencies are supposed to be using to protect public health’.<sup>35</sup> In 2008, Dorbeck-Jung concluded in her analysis of the ICH that ‘major challenges are to enhance the legitimacy of its standard-setting activities and to reveal the secrecy of its influence and powers in the regulatory practice’.<sup>36</sup> In essence, it is claimed that the successes of the ICH thrive on a lack of transparency and participation of other interested parties. Berman argues that although the ICH is viewed as having broad ‘epistemic legitimacy’ considering that standards are scientifically up to speed – which explains their global influence – there is a lack of what she calls ‘political legitimacy’.<sup>37</sup> This is due to the far-reaching influence of industry in contrast to a lack of representation of patients in the actual decision-making. These claims with regard to the ICH’s legitimacy will be assessed

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*Studies* (2001), pp. 347-367; G. de Búrca, ‘Developing Democracy Beyond the State’, 46(2) *Columbia Journal of Transnational Law* (2008), pp. 221-278, p. 224.

<sup>28</sup> M. Shapiro, ‘Administrative Law Unbounded: Reflections on Government and Governance’, 8(2) *Indiana Journal of Legal Studies* (2001), pp. 369-377, p. 374.

<sup>29</sup> W. Mattli, ‘The Politics and Economics of International Institutional Standards Setting: An Introduction’, 8(3) *Journal of European Public Policy* (2001), pp. 328-344, p. 331; J. Mendes, ‘EU Law and Global Regulatory Regimes: Hollowing Out Procedural Standards?’, 10(4) *International Journal of Constitutional Law* (2012), pp. 988-1022.

<sup>30</sup> J. Pauwelyn, ‘Informal International Lawmaking: Mapping the Action and Testing Concepts of Accountability and Effectiveness’, CTEI Working Papers, CTEI-2011-05, (2011), p. 3.

<sup>31</sup> Scott (2010), p. 116.

<sup>32</sup> C. Hodgkin, ‘International Harmonisation – The Need for Transparency’, 9(3) *International Journal of Risk & Safety in Medicine* (1996), pp. 195-199, p. 196.

<sup>33</sup> K. Timmermans, ‘Harmonization, Regulation, and Trade: Interactions in The Pharmaceutical Field’, 34(4) *International Journal of Health Services* (2004), pp. 651-661, p. 651.

<sup>34</sup> J. Abraham & T. Reed, ‘Trading Risks for Markets: The International Harmonization of Pharmaceuticals Regulation’, 1(3) *Health, Risk and Society* (2001), pp. 113-128, p. 125.

<sup>35</sup> J. Abraham, ‘The Pharmaceutical Industry as a Political Player’, 360(9344) *The Lancet* (2002), pp. 1498-1502, p. 1500.

<sup>36</sup> Dorbeck-Jung (2008), p. 71.

<sup>37</sup> A. Berman, ‘The Public-Private Nature of Harmonization Networks’, CTEI Working Paper, CTEI-2011-06, (2011), p. 55.

throughout this research.

These critical remarks about the legitimacy of the ICH are exemplary of concerns raised with regard to global standard-setting in general. The risks and market structures faced today drive regulatory decision-making to the international plane, whereas the required legitimization through democratic institutions is not readily available once the confines of the (democratic) nation states are left behind.<sup>38</sup> Therefore, it has been argued that global governance suffers from a democratic deficit.<sup>39</sup>

These concerns of legitimacy might also affect the EU where it implements such standards into its regulatory framework. Whereas the voluntary nature of standards may suggest that such a legitimacy deficit might not be problematic, it is argued in this research that although global standards are non-binding, their influence on European risk regulation is not to be underestimated. Indeed, although the implementation of international standards is voluntary for the states participating in standard-setting, *de facto* states tend to implement global standards.<sup>40</sup> Once implemented, they can lead to a shift in the requirements of proof for a regulated product,<sup>41</sup> like a presumption of conformity with legislative requirements where products are in accordance with a specific standard. Therefore, after the global standards are implemented in a specific regulatory framework, they have an impact on the rights of individuals, such as companies producing the regulated product or consumers of such products.<sup>42</sup> Thus, although global standards are voluntary instruments, they increasingly influence not only the sovereignty of states but also the rights of individuals, which induces a need to assess the legitimacy of such standards. Where such standards are then implemented in the European framework, they may undermine the legitimacy of the European risk regulation framework if they do not fulfil the procedural requirements applicable to risk regulation in the EU, as this research will argue.

The need for enquiring the legitimacy of global standards and a careful assessment of the decision-making process on the global level is intensified, where standards are not only coordinating the interconnectability or compatibility of products like plugs or tubes, but where these standards govern the safety of products and are of a protective nature, guarding public health or the environment.<sup>43</sup> Especially as risks are not unilaterally perceived in the same way, they are 'instable'<sup>44</sup> and the diverse approaches to their definition and chosen forms of regulation are caused by differences in the social and cultural context and,

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<sup>38</sup> C. Joerges, 'Law, Science and the Management of Risks to Health at the National, European and International Level: Stories on Baby Dummies, Mad Cows and Hormones in Beef', 7(1) *Columbia Journal of European Law* (2001), pp. 1-20, p. 3. See also: Habermas (1998), p. 94 and p. 109f.; O. Dilling, M. Herberg & G. Winter, 'Introduction – Exploring Transnational Administrative Rule-Making', in O. Dilling, M. Herberg & G. Winter (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 1-19, p. 2. On the difficulty of achieving democratic legitimization on the international level: J. Weiler, 'The Geology of International Law – Governance, Democracy and Legitimacy', 64(3) *Zeitschrift für ausländisches öffentliches Recht und Völkerrecht* (2004), pp. 547-562, p. 561. For a counterargument of not discarding democratic legitimacy at the international level and increasing democracy: de Búrca (2008), p. 237.

<sup>39</sup> Hachez & Wouters (2011), p. 683.

<sup>40</sup> See also: D. Kerwer, 'Rules that Many Use: Standards and Global Regulation', 18(4) *Governance* (2005), pp. 611-632.

<sup>41</sup> Röhl (2007), p. 337f.

<sup>42</sup> Mendes (2012), pp. 988-1022; Mendes (2014), pp. 370-401.

<sup>43</sup> Scott (2010), p. 116.

<sup>44</sup> J. Black, 'The Role of Risk in Regulatory Processes', in R. Baldwin, M. Cave & M. Lodge (Eds.), *The Oxford Handbook of Regulation* (Oxford: Oxford University Press, 2010), pp. 302-348, p. 321.

additionally, might be subject to change over the course of time.<sup>45</sup> Therefore, the regulation of risk exceeds mere questions of technicalities, containing certain political or normative choices, which require a legitimate basis.<sup>46</sup>

A look beyond the voluntary nature of global standards is necessary for a comprehensive assessment of global standards and their effects on the EU regulatory system. The global standard-setting bodies and their decision-making procedures need to be assessed in terms of basic administrative procedural standards, such as participatory openness, transparency of the standard-setting process, and independence of the expertise that the bodies claim to possess.<sup>47</sup> Crucial to an assessment of global pharmaceutical standards will therefore be the institutional structure and decision-making process of the global standard-setting body, which will provide insights into the legitimacy of the standards set.<sup>48</sup>

This raises several sub-questions to the research question above, which will be answered with regard to global standards in general and specifically on the pharmaceutical standards set by the International Council for Harmonisation:

- How can the ICH be qualified in legal terms?
- What is the legal nature of ICH standards?
- How can the legitimacy of ICH standards be conceptualised?
- How does the EU implement ICH standards?
- Can the implementation of ICH standards be reconciled with legitimacy requirements in EU risk regulation?

### 3. RESEARCH METHODOLOGY

The research approaches global standards from a EU law perspective, while also taking into account relevant provisions of international law, in order to pay tribute to the multi-level nature of the research question, which is concerned with the implementation of global pharmaceutical standards in the EU. This is carried out as desk research of the relevant legal sources of legislation, case law and legal doctrine. The research combines a theoretical analysis of global standards qua institutional setting, legal qualification and legitimacy, including a discussion of the relevant literature, with the in-depth study of global standard-setting for pharmaceuticals through a public-private initiative.

Along with the study of legal doctrine and a variety of official documents, the research is supplemented by semi-structured qualitative interviews with officials from the European Commission, the European Federation of Pharmaceutical Industries and Associations (EFPIA), the European Medicines Agency (EMA), as well as the German Federal Institute for Drugs and Medical Devices (BfArM). Interviews were conducted with EMA officials involved in the ICH process. A separate interview with officials of the EMA's Legal Department also took place.<sup>49</sup> These interviews were conducted in order to verify the insights obtained and to enquire whether the 'law in books' matched the 'law in action'.<sup>50</sup> In

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<sup>45</sup> Alemanno (2013), p. 38.

<sup>46</sup> Habermas (1998), p. 164f.

<sup>47</sup> Röhl (2007), p. 339.

<sup>48</sup> Scott (2010), p. 112.

<sup>49</sup> The footnotes therefore make a distinction between 'EMA official' on the one hand and 'EMA Legal Department' on the other hand. This should only be seen as a reflection of the separate interviews and does not indicate a difference of position.

<sup>50</sup> R. Pound, 'Law in Books and Law in Action', 44(1) *American Law Review* (1910), pp. 12-44.

this regard, where reference to such interviews is made, they should be regarded as a means to infuse the theoretical research with practical understanding, rather than as evidence for a certain assumption.<sup>51</sup>

Although the legitimacy problems identified in the literature arise on a global level, this research is conducted with an explicitly European perspective. In addition to examining the interaction of regulators at the global level, it analyses the implementation of global pharmaceutical standards in the EU. It aims to provide an in-depth analysis of the regulatory processes on a global level, especially in terms of transparency, participation, and the use of (independent) expertise. Furthermore, it points out the influential role of these pharmaceutical standards on European risk regulation and questions the legitimacy of their implementation.

Moreover, it will provide recommendations to improve the global standard-setting process, based on a comparison with procedural requirements in the European Union. This is not meant to depict European risk regulation and the procedural requirements laid down by European administrative law as an ideal system, but rather to use the lessons learned in the European harmonisation process as inspiration for enhancing global harmonisation through standard-setting. This approach is clarified in Chapter 2. This research is particularly important because while risk regulation beyond the nation state has become a growing field of research, the interface between global bodies adopting certain standards and the domestic systems that have to implement them into their regulatory framework is still not sufficiently understood.

#### 4. RESEARCH STRUCTURE

Chapter 1 introduces global standards and clarifies the complex institutional setting of global standard-setting bodies. The chapter starts with the definition of global standards and identifies their addressees. The legal status of these standards is analysed. The institutional landscape of global standard-setting is examined. The analysis focuses on the actors involved in global standard-setting – regulators and private parties – as well as the forms of institutionalisation. Finally, the role of the EU as actor in the standard-setting process is analysed.

Chapter 2 is devoted to establishing a framework for the legitimacy assessment of global standards. The chapter starts by applying the well-known theory of input and output legitimacy developed by Scharpf. Although output legitimacy is often relied on to justify global standard-setting it does not provide a solution for the legitimacy questions faced in global risk regulation. The research turns to Weber's notion of legal-rational legitimacy in order to establish an analytical framework. This leads to the search for the 'law' capable of providing the relevant basis for the legal-rational legitimacy. The Global Administrative Law and International Administrative Law scholarship is discussed, with particular regard to the question of sources of administrative law applicable to global standard-setting bodies. Finally, taking a European perspective and applying European administrative law is suggested. It is advocated that European administrative law can provide inspiration to form a global administrative law.

Chapter 3 is devoted to the study of pharmaceutical regulation in the EU. The EU's history of harmonisation is described, and the *status quo* of pharmaceutical regulation is introduced. The marketing authorisation procedure in the European Union is explained, providing the background to understand how global standards are used in the EU.

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<sup>51</sup> J. Baldwin & G. Davis, 'Empirical Research in Law', in P. Cane & M. Tushnet (Eds.), *The Oxford Handbook of Legal Studies* (Oxford: Oxford University Press, 2003), pp. 880-900, p. 892.

Moreover, the chapter closely examines the role of soft law measures in the pharmaceutical regulation of the Union.

Chapter 4 introduces the International Council for Harmonisation and its history, mandate and membership. It closely examines the ICH's institutional structure and legal nature. It goes on to analyse ICH guidelines as an outcome of the ICH process regarding the applied standard-setting procedure, the typology of guidelines and, finally, their legal nature.

Chapter 5 identifies the route through which ICH standards are implemented in the European Union. The adoption of ICH Guidelines as Guidelines of the European Medicines Agency is studied. It is shown that the ICH guidelines also have an impact on other aspects of the EU's pharmaceutical regulation framework. The impact of the guidelines on Commission guidelines and binding legislation is thereby identified. A separate section is devoted to the Common Technical Document (CTD), a harmonised marketing authorisation format developed by the ICH. Attention is also paid to the use of ICH standards in court.

Following on from the analysis in Chapters 3, 4 and 5, Chapter 6 considers the legitimacy questions that ICH standards face, applying the analytical framework developed in Chapter 2. The application of procedural standards of participation, independence of expertise, and transparency in the ICH are critically investigated. With regard to each of these principles, European Administrative Law and specifically the procedural standards governing pharmaceutical regulation in Europe are applied to the ICH, testing the compatibility of the standard-setting process with European procedural norms. This analysis leads to suggestions for changes to the ICH process by 'uploading' European administrative law norms to the global level.

Chapter 7 examines whether the legitimacy flaws identified in Chapter 6 carry over to the regulatory framework of the EU through the implementation of the standards and if they can be remedied within the European Union. It examines whether the Commission and the European Medicines Agency, as main actors in the interface between ICH standards and EU pharmaceutical regulation, are subject to political accountability in the EU. It evaluates whether legal accountability in the form of judicial review could address eventual discrepancies between ICH practice and the procedural standards that European administrative law requires. A potential juridification of the interplay between global standards and European pharmaceutical regulation is discussed.

The Conclusion then summarises the findings of Chapters 1-7 and puts them in the larger context of the rise of global standards and their implementation into European risk regulation.



# Chapter 1: Global standards in EU risk regulation – complex regulatory structures for complex risks

## 1. INTRODUCTION

The regulation of products circulating in the internal market is no longer exclusively an internal European Union matter, but has been subject to significant external influences as global standards are implemented in the EU. Such global standards are prominent in the EU's regulatory framework for pharmaceuticals, but also in many other regulatory areas. The regulation of the EU's internal market in the globalised world, therefore, is characterised by substantial interaction between regulatory measures adopted on the global level and the EU level.

This chapter will scrutinize the phenomenon of global standard-setting, while focusing on the interaction of global standards with EU law through the implementation of global standards in the EU, and the participation of EU actors in global standard-setting. It will therefore also provide an introduction to the complex regulatory structures that have developed on a global level. This chapter intends to provide a general introduction of the use of global standards in EU risk regulation and will establish the context for the analysis of the use of global pharmaceutical standards in the Union's regulatory framework.

Global standards are not merely implemented in the EU, but European administrative bodies also actively participate in forming regulatory measures on the global level. This has to be evaluated in the context of the growing cooperation of administrative bodies as a response to the globalisation of the markets that they are mandated to control.<sup>1</sup> Increasing attention on the role of the EU as 'global actor'<sup>2</sup> concerns the EU as a power in global politics<sup>3</sup> as well as the participation of the EU in international organisations.<sup>4</sup> On the other hand, attention has also been paid to the EU's influence on the forming of regulatory norms and governance in different policy areas.<sup>5</sup> However the assessment from the perspective of regulatory cooperation is largely under-theorised, specifically an analysis of the EU bodies as

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<sup>1</sup> See e.g.: C. Möllers, 'Transnationale Behördenkooperation – Verfassungs- und völkerrechtliche Probleme transnationaler administrativer Standardsetzung', 65(2) *Zeitschrift für ausländisches öffentliches Recht und Völkerrecht* (2005), pp. 351-389.

<sup>2</sup> M. Cremona, 'The Union as Global Actor: Roles, Models and Identity', 41(2) *Common Market Law Review* (2004), pp. 553-573; J. Howorth, 'The EU as a Global Actor: Grand Strategy for a Global Grand Bargain?', 48(3) *Journal of Common Market Studies* (2010), pp. 455-474; B. van Vooren & R. Wessel, 'The EU as Global Legal Actor', in B. van Vooren & R. Wessel (Eds.), *EU External Relations Law – Text, Cases and Materials* (Cambridge: Cambridge University Press, 2014), pp. 1-34.

<sup>3</sup> C. Bretherton & J. Vogler, *The European Union as Global Actor*, 2<sup>nd</sup> Edition (Oxon/New York: Routledge, 2006).

<sup>4</sup> P. Eeckhout, *EU External Relations Law*, 2<sup>nd</sup> Edition, (Oxford: Oxford University Press, 2011), pp. 222-231; J. Wouters, J. Odermatt & T. Ramopoulos, 'The EU in the World of International Organizations: Diplomatic Aspirations, Legal Hurdles and Political Realities', Leuven Centre for Global Governance Studies, Working Paper 121, September 2013.

<sup>5</sup> D. Bach & A. Newman, 'The European Regulatory State and Global Public Policy: Micro-institutions, Macro-influence', 14(6) *Journal of European Public Policy* (2007), pp. 827-846; B. van Vooren, S. Blockmans & J. Wouters (Eds.), *The EU's Role in Global Governance – The Legal Dimension* (Oxford: Oxford University Press, 2013). The work of Joanne Scott on the extraterritorial application of European law is also relevant: Scott (2014b), pp. 87-125; Scott (2014a), pp. 1343-1380.

global actors in regulatory cooperation, such as the setting of global standards.<sup>6</sup> Therefore, the chapter will also examine the legal framework applicable to the participation of EU administrative bodies in global standard-setting.

This chapter presents a definition of global standards and examines the incentives for regulators to participate in global standard-setting in Section 2. Based on this definition, Section 3 evaluates the legal nature of standards under the concept of soft law, and also discusses the implementation methods for global standards into European law. Section 4 is devoted to an analysis of the institutional landscape of global standard-setting. It will introduce the actors engaged in global standard-setting (Section 4.1), a typology of global standard-setting bodies (Section 4.2), and place global standards within the context of global governance (Section 4.3). Finally, the legal framework applicable to the participation of the EU in global standard-setting bodies is examined in Section 5.

## 2. EU RISK REGULATION IN A GLOBALISED WORLD

Risks related to the food we eat, the products we use and the medicines we take have become a significant factor in shaping the reality of our day-to-day lives. Consequently, the prevention of the realisation of risks through regulation has become an essential mission for governments around the world.<sup>7</sup> The significance of risk in government action has led some to argue Majone's 'regulatory state'<sup>8</sup> has been overcome, and is nowadays more aptly described as the 'risk regulatory state'.<sup>9</sup> Risk regulation refers to a broad range of measures taken in order to prevent risks to human health from materialising.<sup>10</sup> Furthermore, the concept of risk and the central role assigned to science within it has been immensely influential on the understanding of regulatory action in modern government. Risk is invoked to justify regulation. The determination and approach to counteract risk increasingly shapes how measures will be drafted and by whom, as well as to whom regulators should be accountable.<sup>11</sup>

The regulation of the European Union's internal market, and specifically the regulation of risks related to goods that move freely within this market, is subject to change. It has evolved from being largely enshrined in legislation to a regulatory framework with diverse forms of acts, which are adopted by miscellaneous actors, as administrative bodies and private actors as co-regulators shape the regulatory framework.<sup>12</sup> At the same time, the EU has experienced a 'progressive externalization (and internationalization) of many EU policies

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<sup>6</sup> This gap has also been identified by other authors. See: H. Hofmann, 'Seven Challenges for EU Administrative Law', 2(2) *Review of European Administrative Law* (2009), pp. 37-59, p. 55; C. Möllers & J. Terhechte, '§40 Europäisches Verwaltungsrecht und Internationales Verwaltungsrecht', in J. Terhechte (Ed.), *Verwaltungsrecht der Europäischen Union* (Baden-Baden: Nomos, 2011), pp. 1437-1452, p. 1445.

<sup>7</sup> Alemanno (2013), p. 38.

<sup>8</sup> G. Majone, 'The Rise of the Regulatory State in Europe', 17(3) *West European Politics* (1994), pp. 77-101.

<sup>9</sup> Black (2010), p. 302.

<sup>10</sup> Some other authors like Wiener take a broader approach, including risks to society which are not risks to public health, like terrorism (see: J. Wiener, 'The Rhetoric of Precaution', in J. Wiener et al. (Eds.), *The Reality of Precaution: Comparing Risk Regulation in the United States and Europe* (London: Routledge, 2011), pp. 3-39).

<sup>11</sup> Black (2010), p. 303.

<sup>12</sup> For a comprehensive account see: H. Hofmann, 'Agencies in the European Regulatory Union', TARN Working Paper 5/2016 (June 2016), available via: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=2804230](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2804230), last accessed: 3 April 2017.

and programmes',<sup>13</sup> which ultimately also leads to the absorption of global standards in various areas of European risk regulation. For example, Wouters and Verhoeven identify influences on European law of standards set by the Codex Alimentarius Commission, the International Office of Epizootics and the Secretariat of the International Plant Protection Convention, the Basel Committee on Banking Supervision, the Financial Action Task Force, as well as the United Nations Economic Commission for Europe.<sup>14</sup>

### 2.1 *The Union's reliance on global standards*

Although the implementation of global standards in the European Union has certainly increased in the era of globalisation, it is not a new phenomenon. Already in the Beer Purity case of 1984 the Court obliged Member States to take into account 'the findings of international scientific research, and, in particular the work of the Community's Scientific Committee for Food, the Codex Alimentarius Committee of the FAO and the World Health Organisation'.<sup>15</sup> The obligation to integrate the standards set by a global body concerned with foodstuffs, the Codex Alimentarius Commission, into the risk regulation within the Member States shows that the Court realised early on that regulatory systems – global, European and national – do not function in isolation. Moreover, especially in the EU setting, the reliance on standards presents a presumably objective scientific solution in conflicts between internal market policy and public health protection.

Nowadays the obligation to take account of global standards is deeply rooted in various legal measures of the EU. For example, Article 5(3) of the General Food Law sets out that international standards need to be taken into consideration when passing or amending EU legislation in this field.<sup>16</sup> The preamble of the REACH Regulation for chemicals also states, on the one hand, that the European Chemicals Agency should contribute to global harmonisation initiatives, and, on the other hand, take international standards into account.<sup>17</sup> With regard to pharmaceuticals, the preamble of Regulation 726/2004 establishing the European Medicines Agency envisages a role for 'the Agency to participate actively in international scientific dialogue and to develop certain activities that will be necessary, in particular regarding international scientific harmonisation and technical

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<sup>13</sup> M. Groenleer & S. Gabbi, 'Regulatory Agencies of the European Union as International Actors: Legal Framework, Development over Time and Strategic Motives in the Case of the European Food Safety Authority', 4(4) *European Journal of Risk Regulation* (2013), pp. 479-492, p. 481.

<sup>14</sup> Wouters & Verhoeven (2006), pp. 256-273.

<sup>15</sup> Case 178/84 *Commission v. Germany*, ECLI:EU:C:1987:126, para. 52. See also: E. Vos & C. Joerges, 'Structures of Transnational Governance and their Legitimacy', in J. Vervaele (Ed.), *Compliance and Enforcement of European Union Law* (London: Kluwer, 1999), pp. 71-93, p. 90.

<sup>16</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority, and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24, Art. 5(3).

<sup>17</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93, and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC, and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849, Preamble para. 109.

cooperation (...).<sup>18</sup>

The important role of global standards in EU risk regulation is thus not only a momentary observation of a factual development, but a longstanding policy promoted by the Court and incorporated into legislation. Instead of being a process that only materialises in the back-chambers of regulatory authorities, the incorporation of global standards is openly promoted in the EU. The European Commission also published a Communication in 2006 called ‘Global Europe’, declaring that the Union ‘must play a leading role in sharing best practice and developing global rules and standards. To do so effectively we must also take account of the external dimension in making our regulatory and other standards’.<sup>19</sup> In 2010 the Commission stated that ‘enhanced regulatory cooperation – both in order to promote equivalence or convergence (of rules, standards, testing and certification practices) internationally and to minimize unnecessary costs in regulation worldwide – is an important aspect of our trade relationships’.<sup>20</sup>

The EU’s reliance on global standards follows the rationale that harmonisation of regulatory requirements through global standards is beneficial for regulators as well as the regulated industries. The harmonisation of standards facilitates barrier-free worldwide trade in products, relieving producers from the duty of having to repeatedly adapt their products to differing national standards, and considerably decreasing production costs.<sup>21</sup> Apart from the general economic and political necessity there is another potential gain. Participating authorities benefit from global standard-setting as it responds to the increased need for very specific expertise in the regulation of highly technical areas. Bundling regulatory competences on a global level allows for cost-sharing and prevents the duplication of efforts.<sup>22</sup> Another factor making global standards attractive, at least for governments with important markets, is the potential to achieve a strong influence on the standards agreed upon, and make those standards applicable worldwide.<sup>23</sup>

The move to global standard-setting should also be seen in the context of efforts to address the decrease in consumer confidence that regulators face, caused by several incidents of regulatory failure. In the EU the BSE crisis in particular has left consumers with distrust

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<sup>18</sup> Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use, and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 136, 30 April 2004, pp. 1-33, Preamble (27).

<sup>19</sup> European Commission, ‘Global Europe: competing in the world’, COM(2006) 567, 4 October 2006, p. 9. See also: M. Cremona, ‘Expanding the Internal Market: An External Regulatory Policy for the EU?’, in B. van Vooren, S. Blockmans & J. Wouters (Eds.), *The EU’s Role in Global Governance – The Legal Dimension* (Oxford: Oxford University Press, 2013), pp. 162-177.

<sup>20</sup> European Commission, ‘Trade, Growth and World Affairs – Trade Policy as a Core Component of the EU’s 2020 Strategy’, COM(2010) 612, 9 November 2010, p. 7.

<sup>21</sup> Wouters & Verhoeven (2006), p. 261.

<sup>22</sup> See: Section 4.1.1.

<sup>23</sup> In the pharmaceuticals sector this is a declared goal of the Commission, as it announced: ‘Establishing and enforcing international public health standards is essential to minimise the risk that unsafe products enter the EU market. The work carried out with the US and Japan at the International Conference on Harmonisation (ICH) is essential in this context and must be expanded. ICH standards should be promoted so that they can become worldwide standards.’ See: European Commission, Communication from the Commission to the Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector, COM(2008) 666 final, Brussels, 10 December 2008, p. 13.

in the ability of public authorities to prevent the manifestation of risks.<sup>24</sup> Setting-standards on the global level in this context can thus be viewed as an attempt to reassure the consumer that the standards set represent worldwide expertise as a sign of inclusiveness and quality.<sup>25</sup> Additionally, it allows for the assessment of data collected in various geographic areas, which can be an important contribution to assess the factors leading to a risk emerging.

## 2.2 *Defining global standards: risk regulation through voluntary expertise-based rules*

The reliance on standards as regulatory tools in the EU has already received academic attention. However, a specific type of standards, the so-called ‘European Standards’, have so far formed the focus of scholarly debate with regard to standards in the EU.<sup>26</sup> This standard-setting practice under the New Approach entails that the setting of technical standards has been outsourced through the delegation of standard-setting power from the Commission to three private standard-setting bodies: the European Committee for Standardisation (CEN), the European Committee for Electrotechnical Standardisation (Cenelec), and the European Telecommunications Standards Institute (ETSI).<sup>27</sup>

This research focuses on pharmaceutical standards which govern the quality, safety and efficacy of medicinal products and, therefore, fall within the area of risk regulation. Such risk regulation measures form an important part of legislative and administrative action as risks – defined as the probability that adverse effects are induced by nature or by human action –

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<sup>24</sup> M. Everson & E. Vos, ‘European Risk Governance in a Global Context’, in E. Vos (Ed.), *European Risk Governance - Its Science, its Inclusiveness and its Effectiveness*, Connex Report Series No 6 (2008), pp. 7-36; M. Everson & E. Vos, ‘The Scientification of Politics and the Politicisation of Science’, in M. Everson & E. Vos (Eds.), *Uncertain Risks Regulated* (Oxon: Routledge-Cavendish, 2009), pp. 1-18.

<sup>25</sup> Specifically for the case of pharmaceuticals see: P. Lezotre, *International Cooperation, Convergence and Harmonization of Pharmaceutical Regulations – A Global Perspective* (Oxford/San Diego: Academic Press Elsevier, 2014), p. 173.

<sup>26</sup> In the European Union standards became a popular tool of regulation with the introduction of the ‘New Approach’ in 1985. Whereas before, different categories of products and hazards had been dealt with within individual Directives, now Directives covered a whole sector and only contained ‘essential requirements’, the details of which would be clarified through voluntary standards. The standards set by these bodies are published in the *Official Journal of the European Union*. Although these European standards are voluntary, compliance with them leads to the rebuttable presumption that the product also complies with the responding Directive. Selected publications in the area are: H. Schepel, *The Constitution of Private Governance – Product Standards in the Regulation of Integrating Markets* (Oxford: Hart, 2005); C. Joerges, H. Schepel & E. Vos, ‘The Law’s Problems with the Involvement of Non-Governmental Actors in Europe’s Legislative Processes: The Case of Standardisation under the ‘New Approach’’, EUI Working Paper Law No 99/9, October 1999; G. Brüggemeier, J. Falke, C. Joerges & H. Micklitz (Eds.), ‘Special Issue: European Product Safety, Completion of the Internal Market and the New Approach to Technical Harmonisation and Standards – Reissued’, 6(2) *Hanse Law Review* (2010); R. van Gerstel & H. Micklitz, ‘European Integration through Standardization: How Judicial Review is Breaking Down the Club House of Private Standardization Bodies’, 50(1) *Common Market Law Review* (2013), pp. 145–181; H. Schepel, ‘The New Approach to the New Approach: The Juridification of Harmonized Standards in EU Law’, 20(4) *Maastricht Journal of European and Comparative Law* (2013), pp. 521-533.

<sup>27</sup> Regulation (EU) No 1025/2012 of the European Parliament and of the Council of 25 October 2012 on European standardization, OJ L 316, 25 October 2012, pp. 12-33.

have become an inherent feature of modern reality.<sup>28</sup> Ulrich Beck coined the term ‘risk society’ in referring to this increased significance of risk as a consequence of scientific and technological progress.<sup>29</sup> As a response, risk regulation aims at identifying and preventing harm to human or animal health and the environment.<sup>30</sup>

In this context, regulation should be understood to refer to a broader array of measures, including but not limited to law. Although admittedly ‘regulation’ and ‘law’ are subject to a multitude of definitions, ‘law’ is limited to measures with legally binding effect,<sup>31</sup> while ‘regulation’ as an umbrella term also covers non-binding measures, which are not necessarily devised by public authorities.<sup>32</sup> Regulation can thus be made up of an array of not only legislative but also administrative and technical measures in various forms which can be legally binding or not.<sup>33</sup>

It thereby also encompasses measures, which private actors increasingly take an important part in forming, as governments depend on external expertise in the face of the multitude and intricacy of risks, as will become clear throughout this research. The effort to regulate is complicated since some risks are ‘uncertain’ or unpredictable due to a lack of scientific knowledge.<sup>34</sup> The risks that society faces are increasingly complex in terms of the causes that trigger them, and the interconnected factors and interactions influencing their materialisation.<sup>35</sup> Through the globalisation of markets and mobility of products and people, regulation on a purely national level ceases to efficiently address these risks.<sup>36</sup> Therefore, global standards gain increasing importance as regulatory tools.

Although standards are often colloquially only associated with the compatibility of technical components, they go far beyond this dimension. Global standards appear in a variety of forms, their form and content being largely created through their field of application.<sup>37</sup> Thus, today global standards extend far beyond technical compatibility and

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<sup>28</sup> O. Renn, *Risk Governance – Coping with Uncertainty in a Complex World* (London: Routledge, 2008), p. 1; C. Hood, H. Rothstein & R. Baldwin, *The Government of Risk: Understanding Risk Regulation Regimes* (Oxford: Oxford University Press, 2003), p. 1.

<sup>29</sup> U. Beck, *Risk Society: Towards a New Modernity* (London: Sage, 1992).

<sup>30</sup> See e.g.: Hood, Rothstein & Baldwin (2003), p. 3; K. Zurek, *European Food Regulation after Enlargement: Facing the Challenges of Diversity* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), p. 48. Other authors take a broader approach, including risk to society which are not risks to public health, like terrorism. See: Wiener (2011), pp. 3-39.

<sup>31</sup> J. Habermas, *Between Facts and Norms – Contributions to a Discourse Theory of Law and Democracy* (Cambridge, Massachusetts: MIT Press, 1996), p. 115 and 125.

<sup>32</sup> Black (2002).

<sup>33</sup> Lezotte (2014), p. 1.

<sup>34</sup> E. Fisher, *Risk Regulation and Administrative Constitutionalism* (Oxford/Portland: Hart Publishing, 2010), p. 7; Everson & Vos (2009), p. 3.

<sup>35</sup> Black (2002), p. 3.

<sup>36</sup> For a similar observation in terms of broader policy issues such as pollution or organised crime see: A. Peters, L. Koechlin & G. Fenner Zinkernagel, ‘Non-state Actors as Standard Setters: Framing the Issue in an Interdisciplinary Fashion’, in A. Peters, L. Koechlin, T. Förster & G. Fenner Zinkernagel (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009a), pp. 1-32, p. 1f.

<sup>37</sup> Abbott & Snidal (2001), pp. 345-370. For more information on standards as regulatory tools in various policy field see for example: S. Charnovitz, ‘International Standards and the WTO’, GW Law Faculty Publications & Other Works, Paper 394, (2005); E. Fisher, ‘Drowning by Numbers: Standard-Setting in Risk Regulation and the Pursuit of Accountable Public Administration’, 20(1) *Oxford Journal of Legal Studies* (2000), pp. 109-130; Kerwer (2005), pp. 611-632; H. Morais, ‘The Quest for International Standards: Global Governance vs. Sovereignty’, 50(4) *University of Kansas Law Review* (2001-2002), pp. 779-821.

have evolved into important regulatory tools for organising markets and regulating risks.<sup>38</sup> In the context of risk regulation, standards regulate the safety and quality of products and production processes.<sup>39</sup> While product standards regulate details of a product, as well as its health or safety effect, production standards regulate aspects of a production process.<sup>40</sup>

In this regulatory context a ‘standard’ is defined as a:

‘voluntary expertise based rule,<sup>41</sup> constituting measurable criteria by which a product or a production process or service can be evaluated on the basis of technical or physical conditions’.<sup>42</sup>

Compliance with standards is by definition voluntary, thereby standards constitute a ‘guide for behaviour and for judging behaviour’ in very broad terms.<sup>43</sup> By prescribing certain features, actions, processes, or properties, standards harmonise their area of application. In contrast to mutual recognition agreements they presuppose convergence to one point of reference establishing a specific requirement and the harmonisation of this requirement.<sup>44</sup> Next to the regulation of products, they are also well known in the regulation of finance or labour.<sup>45</sup> In principle such standards can be established on different bases like ‘technical data, ethical considerations, economic forecasts or public concern’.<sup>46</sup>

Generally, depending on the type of standard-setting body, these standards are addressed to governments and/or regulators, economic actors such as companies producing the regulated products and/or other national and international standard-setting institutions.<sup>47</sup> The global standards are often addressed to regulators that are expected to implement them in their regulatory system to harmonise regulatory requirements. However, global standards ultimately have to be taken into account by the regulated industry in the development, testing and production of their products. Thus, such standards, although often addressed to regulators, strongly affect private actors in the end. One can refer to the distinction between ‘first level addressees’ and ‘second level addressees’ used by Goldmann in his categorisation of authoritative acts, which acknowledges that besides the explicit recipients of a measure (‘first level addressees’) the measure may affect other groups (‘second level addressees’)

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<sup>38</sup> D. Kerwer ‘Standardising as Governance: The case of credit rating agencies’, MPI Collective Goods Preprint, No. 2001/3 (2001), p. 7.

<sup>39</sup> Fisher (2010), p. 3; Zurek (2012), p. 48.

<sup>40</sup> K. Nadvi & F. Wältring, ‘Making Sense of Global Standards’, INEF Report Heft 58/2002 (2002), p. 6; W. Mattli & T. Büthe, ‘Setting International Standards: Technological Rationality or Primacy of Power?’, 56(1) *World Politics* (2003), pp. 1-42, p. 3.

<sup>41</sup> Kerwer (2001), p. 8.

<sup>42</sup> Nadvi & Wältring (2002), p. 6.

<sup>43</sup> Abbott & Snidal (2001), p. 345 (emphasis added).

<sup>44</sup> Wouters & Verhoeven (2006), p. 261.

<sup>45</sup> For example, standards in the area of finance are developed through the Basel Committee: M. Savino & M. De Bellis, ‘An Unaccountable Trans-Governmental Branch? The Basle Committee’, in S. Cassese, B. Carotti, L. Casini, E. Cavalieri & E. MacDonald (Eds.), *Global Administrative Law: The Casebook*, 3<sup>rd</sup> Edition, pp. 243-254, available via: <http://www.irpa.eu/wp-content/uploads/2012/08/The-Casebook-Chapter-1.pdf>, last accessed: 3 April 2017. The International Labour Association (ILO) is well-known in the area of labour standards. See: T. Börzel & T. Risse, ‘Public-Private Partnerships: Effective and Legitimate Tools of International Governance?’, in E. Grande & L. Pauly (Eds.), *Complex Sovereignty: On the Reconstruction of Political Authority in the 21st Century* (Toronto: University of Toronto Press, 2007), pp. 195-216.

<sup>46</sup> Fisher (2000), p. 112.

<sup>47</sup> Charnovitz (2005), p. 6.

indirectly, by obliging the first level addressees to ‘impose obligations, grant rights, or change the legal situation of individuals’.<sup>48</sup>

### 3. THE LEGAL NATURE OF GLOBAL STANDARDS: AN ASSESSMENT IN LIGHT OF THE SOFT LAW CONCEPT IN INTERNATIONAL LAW

The definition of global standards used in this research emphasises the voluntary character of these norms. They are not adopted in a legally binding form and are not enforceable against addressees that fail to implement the agreed standards. Still, these standards – at least the ones set by or with the involvement of public authorities – are set in order to harmonise the regulatory frameworks of the respective areas they govern.<sup>49</sup> Therefore, an assessment of the legal nature of global standards as regulatory measures is imperative, given that they do not conform to traditional forms of interaction on a global level, as the next sections will address.

#### 3.1 *The concept of soft law in international law*

Global standards are certainly atypical acts when they are assessed from an international law perspective. In international law agreements only acquire legally binding force where the parties intentionally determine the agreement to be binding, and to confer rights and obligations on the parties governed by international law.<sup>50</sup> The traditional sources of law used at the international level are reflected in Article 38(1) of the Statute of the International Court of Justice, encompassing international conventions, international custom, the general principles of law, as well as – to a limited extent, serving interpretative purposes – case law and scholarly writings.<sup>51</sup>

However, these sources of law do not grasp the complexity of interaction on a global level. States in multi- and bilateral arrangements, as well as international organisations, have diverted from these traditional sources of international law with their strict formation requirements. Here, traditional sources could not sufficiently satisfy the growing need for regulation because they were politically unattainable, or the actors in question lacked the legal capacity to come to binding agreements.<sup>52</sup> In the practice of international relations and the scholarly account thereof, the boundaries between law and non-law are not as clear as Article 38(1) of the ICJ Statute implies. This growing tendency to divert from traditional legal measures goes hand in hand with the diversification of actors and forms of interaction on a global level, as discussed in Section 4. Often these actors do not have the possibility to enact binding international agreements, or prefer softer measures for other reasons.<sup>53</sup>

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<sup>48</sup> M. Goldmann, ‘Inside Relative Normativity: From Sources to Standard Instruments for the Exercise of International Public Authority’, in A. von Bogdandy, R. Wolfrum, J. von Bernstorff, P. Dann & M. Goldmann (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 661-711, p. 687f.

<sup>49</sup> Röhl (2007), p. 319.

<sup>50</sup> O. Schachter, ‘The Twilight Existence of Nonbinding International Agreements’, 71(2) *The American Journal of International Law* (1977), pp. 296-304, p. 296.

<sup>51</sup> Statute of the International Court of Justice, 18 April 1946, Art. 38(1).

<sup>52</sup> M. Knauff, *Der Regelungsverbund: Recht und Soft Law im Mehrebenensystem* (Tübingen: Mohr Siebeck, 2010), p. 258ff.

<sup>53</sup> Knauff establishes a connection between the increase of interacting multilevel legal systems and the rise of soft law. See: Knauff (2010).

Emerging in public international law scholarship, the concept of ‘soft law’<sup>54</sup> was introduced to conceptualise the evolution of international cooperation beyond traditional international law in the form of treaties. Although the academic debate surrounding the concept of soft law has existed since the 1970s,<sup>55</sup> its definition is far from well-established. Most definitions, nevertheless, comprise two elements that are generally used to identify a measure as soft law. First, the measure is not legally binding. Second, although it lacks legally binding force, it still gives rise to – sometimes indirect – legal effects.<sup>56</sup> In this regard Shelton defines soft law broadly as ‘any written international instrument, other than a treaty, containing principles, norms, standards, or other statements of expected behavior’.<sup>57</sup> Nevertheless, the existence and effects of soft law are subject to an intense debate in the scholarship which is far from settled.<sup>58</sup>

One perspective in this debate is the binary or absolute position which argues that the decisive criterion on whether an instrument is to be qualified as law is the question whether a measure is legally binding.<sup>59</sup> Law is created by the legislature of sovereign states and is legally enforceable.<sup>60</sup> Instruments that are not legally binding simply cannot be law and, conclusively, soft law does not exist.<sup>61</sup> At the international level it is established that the sources named in Article 38(1) of the ICJ Statute are binding and, therefore, can be characterised as law. Beyond these sources, according to an absolute view measures are not

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<sup>54</sup> The creation of the term ‘soft law’ is attributed to Lord McNair. See: D. Thürer, ‘Soft Law’, in R. Wolfrum (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: Oxford University Press, 2013), Article last updated March 2009, at para. 5, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.

<sup>55</sup> Knauff (2010), p. 211.

<sup>56</sup> According to Daniel Thürer ‘soft law, as a phenomenon in international relations, covers all those social rules generated by State[s], or together subjects of international law which are not legally binding but which are nevertheless of special legal relevance’. Thürer (2013), Article last updated March 2009, at para. 8, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017. In the European law context, Linda Senden defines soft law as ‘(r)ules of conduct that are laid down in instruments which have not been attributed legally binding force as such, but which nevertheless may have certain (indirect) legal effects, and that are aimed at and may produce practical effects.’ L. Senden, *Soft Law in European Community Law: Its Relationship to Legislation* (Nijmegen: Wolf Legal Publishers, 2003), p. 104. Anne Peters and Isabella Pagotto summarize the definition of soft law in case law and literature as: ‘texts which are on the one hand not legally binding in an ordinary sense, but are on the other hand not completely devoid of legal effects either’. A. Peters & I. Pagotto, ‘Soft Law as a New Mode of Governance: A Legal Perspective’, New Modes of Governance Project Paper 04/D11, (2006).

<sup>57</sup> D. Shelton, ‘Soft Law’, in D. Armstrong (Ed.), *Routledge Handbook of International Law* (Oxon: Routledge, 2009), pp. 68-80, p. 69.

<sup>58</sup> A. Aust, *Handbook of International Law*, 2<sup>nd</sup> Edition, (Cambridge: Cambridge University Press, 2010), p. 11. For a detailed discussion of soft law and an account of the different scholarly approaches to the topic see: Goldmann (2010), pp. 661-711; For a critical perspective on the existence and usefulness of soft law as concept see: J. Klabbers, ‘The Redundancy of Soft Law’, 65(2) *Nordic Journal of International Law* (1996), pp. 167-182; J. Klabbers, ‘The Undesirability of Soft Law’, 67(4) *Nordic Journal of International Law* (1998), pp. 381-391.

<sup>59</sup> M. Bothe, ‘Legal and Non-Legal Norms – A Meaningful Distinction in International Relations?’, 11(65) *Netherlands Yearbook of International Law* (1980), pp. 65-95. See also: G. Shaffer & M. Pollack, ‘Hard and Soft Law’, in J. Dunoff & M. Pollack (Eds.), *Interdisciplinary Perspectives on International Law and International Relations – The State of the Art* (Cambridge: Cambridge University Press, 2013), pp. 197-222.

<sup>60</sup> Habermas (1996), p. 115 and 125.

<sup>61</sup> K. Raustiala, ‘Form and Substance of International Agreements’, 99(3) *The American Journal of International Law* (2005), pp. 581-614, p. 586.

law but politics or morals.<sup>62</sup> This very black-and-white view on law, which protects the normativity of the law against relativisation, is argued to be necessary to protect the essential functioning and force of international law.<sup>63</sup> Accordingly, it has been proposed that the study of measures beyond traditional international law should be left to sociologists and not to lawyers.<sup>64</sup>

Nevertheless, this binary or absolute perspective on international law has not prevented the rise of a variety of measures used by actors on the international plane. Although not conforming to the definition of traditional international law, these measures do have (indirect) legal effects.<sup>65</sup> Opposing the absolute standpoint, from a relativist view on international law it is acknowledged that there is a whole range of instruments, spanning from binding law in the strict sense, to measures having legal effects although they are not legally binding.<sup>66</sup> According to this argumentation there is a scale of legal normativity.<sup>67</sup> It is advocated that 'soft law' begins where measures convey fewer obligations on its drafters than traditional 'hard' law, either through a diminished binding power, less precision and/or the lack of delegation of authority for its interpretation and implementation.<sup>68</sup> A large variety of instruments such as guidelines, principles, codes of practice, recommendations or declarations can fall within this remit.<sup>69</sup> The (indirect) legal effects of these soft law instruments will depend on the function they are intended to fulfil. They find their basis in the fact that state sovereignty means there is a choice of (legal) form for their actions on the international level, both within and beyond their origin in Article 38 of the ICJ Statute.<sup>70</sup>

Thus, in opposition to the binary view of the absolute scholarship, which operates a black-and-white distinction between measures being binding and non-binding, the relativist view acknowledges a spectrum of grey in between. Soft law should nonetheless be distinguished from when there is merely political agreement and thereby where no 'legalisation' whatsoever takes place.<sup>71</sup> Thus, in order to qualify a non-legally binding norm as soft law, it needs to introduce a certain obligation or be subject to an enforcement mechanism.<sup>72</sup>

This research adheres to a relativist rather than a positivist viewpoint. It acknowledges that non-legally binding measures can still constrain parties that agreed on the measure of the freedom to act. This authority conditions their actions, often leaving the possibility of deviation to mere fiction.<sup>73</sup> It is thus accepted that the distinction between legally binding

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<sup>62</sup> Goldmann (2010), p. 671.

<sup>63</sup> P. Weil, 'Towards Relative Normativity in International Law?', 77(3) *American Journal of International Law* (1983), pp. 413-442, p. 441.

<sup>64</sup> Weil (1983), p. 440f.: 'It is one thing for the sociologist to note down and allow for infinite gradations of social phenomena. It is quite another thing for this example to be followed by the man of law, to whom a simplifying rigor is essential.'

<sup>65</sup> Peters & Pagotto (2006), p. 7.

<sup>66</sup> Goldmann (2010), p. 671.

<sup>67</sup> Ibidem.

<sup>68</sup> K. Abbott & D. Snidal, 'Hard and Soft Law in International Governance', 54(3) *International Organization* (2000), pp. 421-456, p. 422; K. Abbott, R. Keohane, A. Moravcsik, A. Slaughter & D. Snidal, 'The Concept of Legalization', 54(3) *International Organization* (2000), pp. 401-419.

<sup>69</sup> Aust (2010), p. 11.

<sup>70</sup> Tietje (2001), p. 257.

<sup>71</sup> Abbott & Snidal (2000), p. 422.

<sup>72</sup> F. Terpan, 'Soft Law in the European Union – The Changing Nature of EU Law', 21(1) *European Law Journal* (2015), pp. 68-96, p. 74.

<sup>73</sup> A. von Bogdandy, P. Dann & M. Goldmann, 'Developing the Publicness of Public International Law', in A. von Bogdandy, R. Wolfrum, J. von Bernstorff, P. Dann & M.

and non-binding measures does not aptly reflect the reality of complex regulatory activity, especially with regard to risk regulation on the global level. Neglecting the existence of soft law would mean attributing a legal-theoretical non-binding character to a large field of regulatory activity that does in fact affect – at least indirectly – the legal situation of a variety of actors, as will be demonstrated in this research.

The reasons why actors adopt legally binding measures instead of opting for soft law are manifold. Generally, soft law is easier to achieve than concrete legalisation as it comes with less costs to sovereignty – namely it encroaches on the state’s freedom to take decisions to a lesser extent.<sup>74</sup> Soft law measures stipulate an opportunity to use very specific and detailed provisions, since states still retain flexibility – at least in legal terms – to deviate.<sup>75</sup> This means that soft law is less likely to be affected by negotiation deadlocks.<sup>76</sup> Moreover, international soft law tools escape the domestic ratification process. The same is true for the use of soft law on the domestic level, where lengthy legislative procedures are bypassed by non-binding measures. Yet the downside to using international soft law as a faster and more flexible regulatory tool is precisely the evasion of democratic control and accountability functions, as exercised through the ratification procedure.<sup>77</sup>

### 3.2 *Global standards as soft law*

Although the soft law debate in public international law often relates to ‘high-politics’ areas like economic law<sup>78</sup> or security,<sup>79</sup> it is also of increasing relevance in technical-administrative cooperation on a global level.<sup>80</sup> As the complexity of risks and interconnection of markets is creating a breeding ground for increased regulatory cooperation, it augments the importance of soft law which has been developed on the global level in risk regulation.

Global risk regulation standards are voluntary measures. They represent the agreement of standard-setting body members on technical and scientific requirements without being legally binding. Accordingly they ‘seek to convince rather than to coerce’.<sup>81</sup> They cannot be qualified using the typology of sources of international law described before. Standards do not gain their influence from hierarchical power but rather gain force through the fact that they are the result of the horizontal cooperation of the concerned parties.<sup>82</sup> Since the standards represent a common agreement of the participating parties on very specific details, the fact that they are the product of regulatory cooperation gives them authority. Moreover, as for all soft law, they certainly entail commitments in accordance with good faith.<sup>83</sup> Thus, although no legal consequences would be attached to a non-implementation of a global

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Goldmann (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 3-32, p. 11f.

<sup>74</sup> Abbott & Snidal (2000), p. 436ff.

<sup>75</sup> A. Boyle, ‘Some Reflections on the Relationship of Treaties and Soft Law’, 48(4) *International and Comparative Law Quarterly* (1999), pp. 901-913, p. 903.

<sup>76</sup> Kerwer (2005), p. 616.

<sup>77</sup> Boyle (1999), p. 903; Goldmann (2010), p. 668.

<sup>78</sup> C. Chinkin, ‘The Challenge of Soft Law: Development and Change in International Law’, 38(4) *International and Comparative Law Quarterly* (1989), pp. 850-866.

<sup>79</sup> An often referred to example of soft law is the final act of the Helsinki Conference on Security and Co-operation from 1975. See: Schachter (1977), p. 296; R. Baxter, ‘International Law in “Her Infinite Variety”’, 29(4) *International and Comparative Law Quarterly* (1980), pp. 549-566, p. 557.

<sup>80</sup> Tietje (2001), p. 255.

<sup>81</sup> Kerwer (2005), p. 611.

<sup>82</sup> Röhl (2007), p. 321.

<sup>83</sup> Boyle (1999), p. 902.

standard in the regulatory practice of a party, this does not mean that the standards are not followed in practice, or that members were completely free to ignore them.<sup>84</sup> Indeed, for all international law – hard or soft – diplomatic and moral pressure is evaluated as an important enforcement tool.<sup>85</sup> It should be stressed that although there is no legal implementation requirement following from the membership in international standard-setting bodies, these very effective regulatory tools can become binding *de facto*. This brings global standards within the remit of the soft law concept.

For the establishment of detailed rules in particular, as with global standards, the benefits of diverging from regulation through ‘hard law’ are manifold, including less sovereignty costs, more flexibility, and a larger likelihood of compromise. The fact that soft law generally escapes the formal internal ratification processes means that the use of soft law in contrast to hard law allows for speedy reactions to developments in science, technology or the environment, which is highly advantageous in risk regulation. Apart from the procedure used to initially establish the soft law measure, the process of changing the terms agreed upon is also swifter compared to amendment procedures of international treaties, or other forms of hard law. This gives soft law the advantage of being easily adaptable to new scientific insights or changes in policy approaches.<sup>86</sup> Moreover where standards are established in informal regulatory cooperation, soft law is often the only available regulatory tool, as the actors lack the capacity to enter into binding commitments under international law.<sup>87</sup>

Additionally, standards in international law have been reinforced through being referenced to in treaties, which has the potential to transform their legal status.<sup>88</sup> For example, the reference to international standards by the Sanitary and Phytosanitary (SPS) Agreement and the Technical Barriers to Trade (TBT) Agreement of the World Trade Organisation (WTO) has given international standards increased importance and influence.<sup>89</sup> The SPS agreement in this regard identifies the Codex Alimentarius Commission, the International Office of Epizootics and the Secretariat of the International Plant Protection Convention as relevant international standard-setting organizations, leaving other

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<sup>84</sup> Schachter (1977), p. 300.

<sup>85</sup> Chinkin (1989), p. 866.

<sup>86</sup> G. Majone, ‘Science and Trans-Science in Standard Setting’, 9(1) *Science, Technology, & Human Values* (1984), pp. 15-22, p. 19; Abbott & Snidal (2000), p. 442. Pointing to the flexibility advantages of soft law measures, Boyle correctly establishes that annexes to binding treaties could provide the same benefit of amenability, but are often not the preferred choice over soft law. . See: Boyle (1999), p. 905.

<sup>87</sup> Knauff (2010), p. 286. This will be further discussed in Section 4.1.

<sup>88</sup> Boyle (1999), p. 906.

<sup>89</sup> WTO, Agreement on the Application of Sanitary and Phytosanitary Measures, 15 April 1994, 1867 U.N.T.S. 493 (1994); WTO, Agreement on Technical Barriers to Trade, 15 April 15, 1994, 1868 U.N.T.S. 120 (1994). See: L. Wallach, ‘Accountable Governance in the Era of Globalization – The WTO, NAFTA and International Harmonization of Standards’, 50(4) *Kansas Law Review* (2001-2002), pp. 823-865; J. Scott, ‘International Trade and Environmental Governance: Relating Rules (and Standards) in the EU and WTO’, 15(2) *European Journal of International Law* (2004), pp. 307-354; A. Herwig, ‘The Contribution of Global Administrative Law to Enhancing the Legitimacy of the Codex Alimentarius Commission’, in O. Dilling, M. Herberg & G. Winter (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 171-212; M. Livermore, ‘Authority and Legitimacy of Global Governance: Deliberation, Institutional Differentiation, and the Codex Alimentarius’, 81(2) *New York University Law Review* (2006), p. 766-801.

organisations to be identified through the SPS Committee.<sup>90</sup>

Article 3.1 of the SPS Agreement and Article 2.4 of the TBT Agreement promote these international standards through an obligation for WTO members to use them as a basis for measures they adopt.<sup>91</sup> Moreover under Article 3.2 of the SPS Agreement and Article 2.5 TBT Agreement, measures of the WTO members in conformity with international standards are presumed to be in accordance with WTO law, although this presumption is rebuttable.<sup>92</sup> ‘Conformity’ in this context has to be read as a full, literal implementation of the international standard into the members’ measure.<sup>93</sup> In addition to these incentives for the implementation of international standards or their use as the basis of national measures, Article 3.3 of the SPS Agreement also contributes to the importance of global standards. It subjects the possibility to introduce or maintain a high level of protection through a national measure in deviation from international standards to situations where this can either be scientifically justified or through a risk assessment and redetermination of the standard of protection in accordance with Article 5 of the SPS Agreement. It is argued that Article 3 of the SPS Agreement in essence makes standards set by the Codex Alimentarius obligatory, or at least *de facto* binding, due to the fact that a diversion from these standards is extremely difficult or even impossible to scientifically substantiate.<sup>94</sup> Thus, although it is true that the standards set by international bodies still need to be transposed and implemented into the members’ legislative framework, the SPS and TBT Agreements have created a system of pressure that renders deviation almost impossible. Indeed, Masson-Matthee observed in her study of the Codex Alimentarius that EU secondary legislation, especially since the coming into force of Regulation (EC) No 178/2002, the Union’s General Food Law,<sup>95</sup> and the full membership of the EU in the Codex, ‘frequently take Codex measures or their scientific basis into consideration, which has led to the adjustment of several EC measures’.<sup>96</sup>

Additionally, although global standards might be qualified as ‘soft law’ measures from an international law perspective, this qualification may change again with the implementation of these standards in the regulatory framework of a state that is party to the standard-setting process.<sup>97</sup> They may be implemented in legislation or used to further define legislative requirements.<sup>98</sup> Some authors argue therefore that in cases where standards define legislative requirements they ‘would be closer to “hard law” than to “soft law”’.<sup>99</sup> Even without legislative enforcement, in some regulated areas it is also common that private companies certify and audit the compliance of certain standards. NGOs can function as watchdogs, contributing to the fact that originally non-mandatory standards are subject to complex

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<sup>90</sup> WTO, Agreement on the Application of Sanitary and Phytosanitary Measures, 15 April 1994, 1867 U.N.T.S. 493 (1994), Art. 3 and Annex A.

<sup>91</sup> See: M. Masson-Matthee, *The Codex Alimentarius Commission and Its Standards* (The Hague: TMC Asser Press, 2007), p. 140ff.

<sup>92</sup> Scott (2004), p. 324; Masson-Matthee (2007), p. 153.

<sup>93</sup> Herwig (2011), p. 177.

<sup>94</sup> Wouters & Verhoeven (2006), pp. 246-273, p. 250; Masson-Matthee (2007), p. 159ff.

<sup>95</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24.

<sup>96</sup> Masson-Matthee (2007), p. 133.

<sup>97</sup> This is exemplified in the next section (section 3.3), which discusses the implementation of global standards in the EU.

<sup>98</sup> Knauff (2010), p. 287.

<sup>99</sup> Morais (2001-2002), p. 781.

control structures, making them less voluntary.<sup>100</sup> In this case, the standards remain non-binding, but are enforced through private actors even without the power of law.

In sum, where the relativity of law is acknowledged, standards may be qualified as soft law. This means that although global standards are per definition voluntary and not legally binding, for every standard-setting body and the standards that it adopts, there must be a case-by-case assessment. Such an assessment must address whether the measures are presenting obligations to the parties taking part in standard-setting and whether they affect the legal situation of their addressees and the objects of regulation, even if indirectly.

### 3.3 *Implementation of global standards in the European Union*

The non-binding nature of global standards also has consequences for their implementation into the regulatory framework of the Union. As a rule, where the European Union concludes international agreements, these are binding upon the EU institutions and Member States according to Article 216(2) TFEU.<sup>101</sup> The European Union integrates the international agreements it concludes through ‘automatic incorporation’,<sup>102</sup> without further transposition requirements in its legal order.<sup>103</sup> Once they have entered into force, the concluded agreements become an integral part of the Union’s legal order.<sup>104</sup> Furthermore, they prevail

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<sup>100</sup> Kerwer (2005), p. 618.

<sup>101</sup> Here, ‘binding’ should be read as legally binding under EU law. This led van Rossem to state that Art. 216(2) TFEU forms ‘the constitutional bridge’ between international and European law. See: J. van Rossem, ‘The EU at Crossroads: A Constitutional Inquiry into the way International Law is Received within the EU Legal Order’, in E. Canizzaro, P. Palchetti & R. Wessel (Eds.), *International Law as Law of the European Union* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), pp. 59-89, p. 66.

<sup>102</sup> M. Mendez, ‘The Legal Effect of Community Agreements: Maximalist Treaty Enforcement and Judicial Avoidance Techniques’, 21(1) *The European Journal of International Law* (2010), pp. 83-104.

<sup>103</sup> The effects of international agreements in the European Union legal order are discussed in literature in detail. See amongst others: A. Peters, ‘The Position of International Law Within the European Community Legal Order’, 40 *German Yearbook of International Law* (1997), pp. 9-78; M. Cremona, ‘External Relations and External Competence of the European Union: The Emergence of an Integrated Policy’, in P. Craig & G. de Búrca (Eds.), *The Evolution of EU Law*, 2<sup>nd</sup> Edition (Oxford: Oxford University Press, 2011), pp. 217-268; Eeckhout (2011), pp. 323-434; C. Kaddous, ‘Effects of International Agreements in the EU Legal Order’, in M. Cremona & B. De Witte (Eds.), *EU Foreign Relations Law: Constitutional Fundamentals* (Oxford/Portland: Hart Publishing, 2008), pp. 291-312; R. Wessel, ‘Reconsidering the Relationship between International and EU Law: Towards A Content-Based Approach?’, in E. Canizzaro, P. Palchetti & R. Wessel (Eds.), *International Law as Law of the European Union* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), pp. 7-33; C. Eckes, ‘International Law as Law of the EU: The Role of the European Court of Justice’, in E. Canizzaro, P. Palchetti & R. Wessel (Eds.), *International Law as Law of the European Union* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), pp. 353-377.

<sup>104</sup> Case 181/73 *Haegeman v. Belgium*, ECLI:EU:C:1974:41, paras. 2-6; Case 104/81 *Hauptzollamt Mainz v. Kupferberg*, ECLI:EU:C:1982:362, paras. 12-17. Moreover, binding as well as non-binding decisions of international bodies necessary for the application of these international agreements, and directly linked to them will also form an integral part of the Union’s law. See: Case 30/88 *Greece v. Commission*, ECLI:EU:C:1989:422, para. 13; Case C-188/91 *Deutsche Shell v. Hauptzollamt Hamburg-Harburg*, ECLI:EU:C:1993:24, para. 17.

over secondary Union law.<sup>105</sup> Such an international agreement can then have direct effect in terms of the individual,<sup>106</sup> if ‘regard being had to its wording and the purpose and nature of the agreement itself, the provision contains a clear and precise obligation which is not subject, in its implementation or effects to the adoption of any subsequent measure’.<sup>107</sup> In this case, the international agreement can be relied on in Court directly without the need for implementing legislation.<sup>108</sup>

However, with regard to global standards, it was already shown in the previous sections that they do not constitute international agreements but soft law in the form of voluntary expertise-based rules. Since they do not take the form of legally binding international agreements, they do not benefit from the automatic incorporation into the European legal order, but instead have to be implemented. These standards will require a connecting measure (*‘Bindungselement’*) to be incorporated into a regulatory framework.<sup>109</sup> For the implementation of global standards into the European framework in principle two routes are open: implementation through binding Union legislation, and implementation via EU administrative soft law measures.

The first route is implementation through a binding legislative measure on an EU level. Article 288 TFEU provides for regulations, directives and decisions as secondary legislative means, which could be used in order to transform a global standard into binding European legislation. Three variations of legislative implementation route can be distinguished: (i) *the binding static reference* to a certain standard in force at the time of implementation, (ii) a *dynamic binding reference*, where a general reference to a certain standard or standard setting-body also includes future developments of this standard or new norms adopted by the standard-setting body, and, (iii) an *obligation to take into account* (as opposed to being bound by) a certain standard or rules of a certain standard-setting body.<sup>110</sup>

Thus, the implementation in variations (i) and (ii) leads to a legislative enforcement of the global standards, making them a part of European Union law through either absorbing the standards into the regulatory framework through (literal) transposition into an EU legislative measure, or through making reference to them in binding legislation. An example for the first variant, the static reference, is Directive 2006/23/EC on a Community air traffic controller licence, which transposes standards set by the International Civil Aviation Organisation (ICAO) and the European Organisation for the Safety of Air Navigation

<sup>105</sup> Case C-61/94 *Commission v. Germany*, ECLI:EU:C:1996:313, para. 52; Case C-286/02 *Bellio F.lli*, ECLI:EU:C:2004:212, para. 33; Case C-344/04 *International Air Transport Association and Others (IATA)*, ECLI:EU:C:2006:10, para. 35.

<sup>106</sup> Direct effect has been acknowledged for plenty of international agreements. However, the Court made an important exception in ruling that GATT/WTO law is not directly effective due to the nature and structure of the agreements. See e.g. Joined cases 21 to 24/72 *International Fruit Company v. Produktschap voor Groenten en Fruit*, ECLI:EU:C:1972:115; Case C-280/93 *Germany v. Council*, ECLI:EU:C:1994:367; Case C-149/96 *Portugal v. Council*, ECLI:EU:C:1999:574; Case C-377/02 *Van Parys v. Belgische Interventie- en Restitutiebureau*, ECLI:EU:C:2005:121. However, the Court has been according indirect effect to these agreements, establishing that where Union law is implementing WTO law or where provisions of Union refer to WTO agreements, the Union measure can be judicially reviewed in the light of WTO law. See: Case 70/87 *Fediol v. Commission*, ECLI:EU:C:1989:254; Case C-69/89 *Nakajima v. Council*, ECLI:EU:C:1991:186.

<sup>107</sup> Case C-12/86 *Demirel* [1987], ECLI:EU:C:1987:400, para. 14.

<sup>108</sup> Peters (1997), p. 44.

<sup>109</sup> Müller-Graff (2012), p. 27.

<sup>110</sup> Müller-Graff (2012), p. 28; M. Ruffert, ‘§17 Rechtsquellen und Rechtsschichten des Verwaltungsrechts’, in W. Hoffmann-Riem, E. Schmidt-Aßmann & A. Voßkuhle (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 1163-1255, p. 1212ff.

(Eurocontrol).<sup>111</sup> The provisions of the Directive transpose and enforce the standards set by these organisations with regard to language requirements, and training of air traffic controllers by incorporating their substance into a legislative measure.<sup>112</sup>

The second variation, the dynamic reference, means that a standard or the output of a certain standard-setting body, is referenced in binding legislation, not only with regard to the standards as adopted at the time the legislative measure is adopted, but also in opening the Union framework for future amendments or new standards. This is exemplified by Directive 2004/36/EC on the safety of third-country aircrafts using Community airports,<sup>113</sup> which is enacted in order to ensure ‘a harmonised approach to the effective enforcement of international safety standards within the Community’<sup>114</sup> and defines these international standards as ‘the safety standards contained in the Chicago Convention and its Annexes, as in force at the time’.<sup>115</sup> With regard to the standards set by the International Maritime Organisation (IMO), the EU has adopted Regulation (EC) No 2099/2002 that amends a whole range of legislative measures in the Union’s maritime legislation, so as to make all references in these measures to international standards dynamic.<sup>116</sup> For all these measures, the ‘applicable international instruments shall be those which have entered into force, including the most recent amendments thereto’.<sup>117</sup> At the same time the Regulation introduces a conformity check procedure, which allows for the prevention of an amendment of an international standard from affecting EU legislation through a comitology procedure.<sup>118</sup> Thus, where an EU maritime law legislative measure includes a reference to the standards set by the IMO, amendments to these standards will become automatically applicable as well, if the Commission has not initiated a conformity checking procedure.

The third variation, an obligation to take into account certain standards, is the more common implementation method with regard to standards, at least in the field of risk regulation. Regulation (EC) 178/2002, which is known as the ‘General Food Law’, exemplifies this variant, as Article 5(3) contains an obligation to take international standards

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<sup>111</sup> Directive 2006/23/EC of the European Parliament and of the Council of 5 April 2006 on a Community air traffic controller license, OJ L 114, 27 April 2006, pp. 22-37. See specifically Preamble (4).

<sup>112</sup> See also: Röhl (2007), p. 333.

<sup>113</sup> Directive 2004/36/EC of the European Parliament and of the Council of 21 April 2004 on the safety of third-country aircraft using Community airports, OJ L 143, 30 April 2004, pp. 76-86. See also: Röhl (2007), p. 334.

<sup>114</sup> Directive 2004/36/EC of the European Parliament and of the Council of 21 April 2004 on the safety of third-country aircraft using Community airports, OJ L 143, 30 April 2004, pp. 76-86, Art. 1.

<sup>115</sup> Directive 2004/36/EC of the European Parliament and of the Council of 21 April 2004 on the safety of third-country aircraft using Community airports, OJ L 143, 30 April 2004, pp. 76-86, Art. 2(b).

<sup>116</sup> Regulation (EC) No 2099/2002 of the European Parliament and of the Council of 5 November 2002 establishing a Committee on Safe Seas and the Prevention of Pollution from Ships (COSS) and amending the Regulations on maritime safety and prevention of pollution from ships, OJ L 324, 29 November 2002, pp. 1-5.

<sup>117</sup> Regulation (EC) No 2099/2002 of the European Parliament and of the Council of 5 November 2002 establishing a Committee on Safe Seas and the Prevention of Pollution from Ships (COSS) and amending the Regulations on maritime safety and prevention of pollution from ships, OJ L 324, 29 November 2002, pp. 1-5, Art. 4.

<sup>118</sup> Regulation (EC) No 2099/2002 of the European Parliament and of the Council of 5 November 2002 establishing a Committee on Safe Seas and the Prevention of Pollution from Ships (COSS) and amending the Regulations on maritime safety and prevention of pollution from ships, OJ L 324, 29 November 2002, pp. 1-5, Art. 5.

into account whenever new food legislation is drafted and adopted in the EU.<sup>119</sup> Moreover, Article 13 of the General Food Law is devoted to encouraging the participation of Member States and the EU in international standard-setting bodies. It contains the obligation to ‘promote consistency between international technical standards and food law while ensuring that the high level of protection adopted in the Community is not reduced’.<sup>120</sup> Following the obligation to take international standards into account when drafting EU food legislation, several legislative measures include references to the Codex or have been adjusted based on Codex standards.<sup>121</sup> The practice of referencing to Codex standards in secondary EU legislation is quite advanced; the legislation explicitly documents where the standards should find application and under which circumstances there can be deviations.<sup>122</sup> This sophisticated framework can probably not be attributed solely to the reference to international standards in the General Food Law, but in all likelihood is also due to the reinforced role of the Codex under WTO law.<sup>123</sup>

In the field of chemicals, for example, the REACH regulation does not foresee a general obligation to take into account global standards. However, the preamble of the REACH regulation states: ‘(t)o promote broad international consensus, the Agency should take account of existing and emerging international standards in the regulation of chemicals, such as the Globally Harmonised System (GHS) of classification and labeling of chemicals’.<sup>124</sup> Moreover, the REACH regulation in Article 13 lays down the general requirements for generation of information on intrinsic properties of substances. Paragraph 3 provides that tests on substances shall be made according to the Commission Regulation or ‘international test methods recognised by the Commission or the Agency as being

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<sup>119</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24, Art. 5(3). This provision allows for the deviation from international standards ‘where such standards or relevant parts would be an ineffective or inappropriate means for the fulfilment of the legitimate objectives of food law, or where there is a scientific justification, or where they would result in a different level of protection from the one determined as appropriate in the Community.’

<sup>120</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority, and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24, Art. 13(e).

<sup>121</sup> Masson-Matthee (2007), p. 123ff.; J. Mendes, ‘Administrative Law Beyond the State: Participation at the Intersection of Legal Systems’, in E. Chiti & B. Mattarella (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer, 2011a), pp. 111-132, p. 120ff.

<sup>122</sup> The General Food Law in Arts. 5(3) and 13(e) for example introduces the condition that the international standard applied might not offer a lower level of protection than set in the Union. Art. 5(3) also allows for deviation where there is a scientific justification, or where the standards are unsuitable for achieving the general aims of the EU food regulation.

<sup>123</sup> See: Section 3.2.; M. Masson-Matthee, ‘The Codex Alimentarius Commission and its Food Safety Measures in the Light of their New Status’, in M. Everson & E. Vos (Eds.), *Uncertain Risks Regulated* (Oxon: Routledge-Cavendish, 2009), pp. 324-388, p. 330.

<sup>124</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849, Preamble para. 109.

appropriate'.<sup>125</sup> Article 13(4) requires that ecotoxicological and toxicological tests are in accordance with good laboratory practice, as established in a Directive or 'other international standards recognised as being equivalent by the Commission or the Agency'.<sup>126</sup> In this case the standards have to be recognised, before a producer can use them as a basis for the tests that are conducted. This, therefore, forms an obligation to take into account international standards in judging the acceptability of test, requiring a prior recognition of these standards by the EU administrative bodies.

Apart from these three variations of the first route of implementation of global standards through legislative measures, the second implementation route maintains the soft law character of global standards after implementation in the EU: implementation via administrative guidelines. Progressively such 'soft administrative rule-making'<sup>127</sup> is gaining importance in the EU's regulatory framework. Administrative bodies frequently use these soft law measures to further clarify legislative requirements. Global standards are often used in EU soft law, in the context of clarification and further definition of technical and scientific requirements in EU law. This is also the implementation method that is adhered to for the pharmaceutical standards forming the focus of this research. Their implementation into the regulatory framework for pharmaceuticals in the European Union is subject to detailed analysis in Chapter 5.

#### 4. THE INSTITUTIONAL LANDSCAPE OF GLOBAL STANDARD-SETTING

While the previous sections were devoted to the definition of global standards and the assessment of their legal nature, this section turns to the institutional landscape of global standard-setting bodies. First of all, it examines the actors engaged in standard-setting on a global level. That analysis is followed by a typology of international standard-setting bodies, with a specific focus on the legal nature of such bodies. As the institutional landscape of global standard-setting is very diverse and ever-changing, this section aims to provide an overview of the phenomenon. It clarifies who is driving the standard-setting processes and provides an insight into the institutional diversity of these bodies.

Rather than being established by national or regional jurisdictions in isolation, the global standards subject to this research originate from the global level. 'Global' should, for this purpose, be understood to refer to standards set beyond the nation state, on what is often termed the 'international' level. However, as the research also specifically takes into account other actors than states, the term global has been chosen over 'international' in order not to delimit the scope to standards set by the cooperation of nation states alone.

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<sup>125</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849, Art. 13(3).

<sup>126</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849, Art. 13(4).

<sup>127</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 14.

‘Global’ more appropriately reflects the interconnection of different levels of regulation – regional, national, international – whereas ‘international’ is more one-dimensional in this sense.<sup>128</sup> Another term that is used in this regard is ‘transnational’. This draws attention to the fact that it is not the state acting as the subject of international law, but rather a sub-state unit such as an regulatory authority. Consequently, ‘transnational’ refers to cases where standards are set not between (or ‘inter’) states, but rather transcend state borders, in cooperation with diverse national bodies that do not necessarily represent the state as such.<sup>129</sup>

These global standards harmonise regulatory systems to create a level playing-field in international trade.<sup>130</sup> They do sometimes originate in bodies with limited membership, confined to certain states, selected for example on geographical or economic criteria.<sup>131</sup> An example of such membership limitation can be found in the OECD, which engages in chemicals standard-setting.<sup>132</sup> Global standards as understood for the purpose of this research should, therefore, not be read as being open to input from all countries or as necessarily universally applicable.

#### 4.1 *Actors engaged in global standard-setting*

Global standard-setting not only deviates from traditional international law in the sense that standards are soft law measures, as discussed in the previous section, but also in the sense that the actors involved in standard-setting are atypical when compared to the traditional state-centred focus of international law. National regulators and private parties are the main actors in the global standard-setting arena. Starting with an examination of global standards originating in the cooperation of regulators in Section 4.1.1, the analysis will turn to the increasing involvement of private actors in global standard-setting in Section 4.1.2.

##### 4.1.1 Global standards as a product of regulatory cooperation

When it comes to the specificities of setting regulatory standards, on the national level it is the competence of the executive to establish the standards in question, due to its power to ‘control, from day to day, the state’s instruments of coercion, wealth and information’.<sup>133</sup> In most jurisdictions, specifically the administration, as part of the executive, will be in charge of the regulation of risks. Where the setting of regulatory standards essentially means the determination of an acceptable risk, the legislator will determine the policy framework and often also the procedure to come to this decision, but it will be the task of the administration, often in the form of unelected expert bodies, to decide on the acceptable risk in setting a specific standard.<sup>134</sup> The setting of regulatory standards can thus be qualified as a

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<sup>128</sup> von Bogdandy, Dann & Goldmann (2010), p. 7.

<sup>129</sup> M. Ruffert, *Die Globalisierung als Herausforderung an das Öffentliche Recht* (Stuttgart: Boorberg, 2004), p. 35.

<sup>130</sup> Morais (2001-2002), p. 790.

<sup>131</sup> Röhl (2007), p. 322.

<sup>132</sup> For the OECD, economic factors are the decisive membership criterion, as it describes itself as encompassing ‘representatives’ of 30 industrialised countries in North America, Europe and the Asia and Pacific region as well as the European Commission. See e.g.: OECD, OECD Series on Testing and Assessment Number 1 – Guidance Document for the development of OECD Guidelines for the testing of chemicals (as revised 2009), 5 August 2009, ENV/JM/MONO(2006)20/REV1, p. 14.

<sup>133</sup> D. Curtin, *Executive Power of the European Union – Law, Practice and the Living Constitution* (Oxford: Oxford University Press, 2009), p. 20.

<sup>134</sup> Fisher (2010), p. 19.

form of ‘executive rule making’.<sup>135</sup> Risk regulation and the setting of regulatory standards thus essentially form administrative tasks of the executive branch of a jurisdiction.

In a traditional understanding of administrative law, administrative power only comprises activities within the legal order of this jurisdiction.<sup>136</sup> However, the risks that the standards examined in this research are aiming to address are complex, in the sense that they are caused by a variety of interacting factors.<sup>137</sup> With the globalisation of international trade in consumer products, these risks transcend national borders.<sup>138</sup> Thus, where in a globalised risk society, the risks transcend state borders, naturally the regulation addressing these risks has to follow suit. Increasingly, risk regulation standards originate in the cooperation of regulatory authorities at a global level. Consequently, a trend away from regulation in nation states towards the evolution of international governance structures can be observed.<sup>139</sup> The cooperation of administrative actors on the international plane takes place in various degrees of formalisation: from cooperation in the form of existing international organisations, through the establishing of new international organisations with an explicit regulatory mandate, to interaction in *fora*, which are not formally established under international law (see Section 4.2).

Admittedly, regulatory cooperation is not limited to the regulation of risk and is not necessarily a phenomenon of the 21st century. Examples of regulatory administrative cooperation can be found as early as in the 19th century.<sup>140</sup> Administrative cooperation often addressed the regulation of infrastructure, such as communication and traffic. For example, the International Telegraphic Union was established in 1865 in order to facilitate an exchange of information between several telegraphic administrators.<sup>141</sup> However, increasing globalisation and the rise of the risk society led to an amplification of regulatory cooperation. As the previous section has shown, this amplification of regulatory cooperation is also deeply interlinked with the increase in non-binding forms of interaction on global level.

The cooperation of administrative bodies at the global level is a phenomenon that was theorised as ‘transgovernmental relations’ in 1974 by Keohane and Nye, defined as ‘sets of direct interactions among sub-units of different governments that are not controlled or closely guided by the policies of the cabinets or chief executives of those governments’.<sup>142</sup>

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<sup>135</sup> Hofmann (2013), p. 423.

<sup>136</sup> See: Tietje (2001) p. 174ff.

<sup>137</sup> Black (2002), p. 3.

<sup>138</sup> For an interdisciplinary study on the links between trade and risks see: M. van Asselt, E. Versluis & E. Vos (Eds.), *Balancing between Trade and Risk – Integrating Legal and Social Science Perspectives* (Oxon/New York: Routledge/Earthscan, 2013).

<sup>139</sup> See e.g.: Möllers (2005a), p. 352ff.; Hofmann (2013), pp. 423-442; Tietje (2001); J. Tallberg, ‘Delegation to Supranational Institutions: Why, How, and with What Consequence’, 25(1) *West European Politics* (2002), pp. 23-46; K. van Kersbergen & F. van Waarden, “Governance” as a Bridge between Disciplines: Cross-Disciplinary Inspiration Regarding Shifts in Governance and Problems of Governability, Accountability and Legitimacy’, 43(2) *European Journal of Political Research* (2004), pp. 143-171.

<sup>140</sup> A. Peters & S. Peter, ‘International Organizations: Between Technocracy and Democracy’, in B. Fassbender & A. Peters (Eds.), *The Oxford Handbook of the History of International Law* (Oxford: Oxford University Press, 2012), pp. 170-197, p. 174ff.; C. Möllers, ‘European Governance: Meaning and Value of a Concept’, 43(3) *Common Market Law Review* (2006), pp. 313-336, p. 319; Tietje (2001), p. 119ff.

<sup>141</sup> C. Tietje, ‘History of Transnational Administrative Networks’, in O. Dilling, M. Herberg & G. Winter (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 23-37, p. 28ff.

<sup>142</sup> R. Keohane & J. Nye, ‘Transgovernmental Relations and International Organizations’, 27(1) *World Politics* (1974), pp. 39-62, p. 43.

Administrative regulators such as national civil servants increasingly cooperate with their counterparts on the global level.<sup>143</sup> This is in contrast to the traditional approach to external relations of states, which used to be centred around ‘one central authority, the foreign office and its diplomatic service’,<sup>144</sup> where the actors usually were Heads of States, government officials or embassy staff.<sup>145</sup> Weiler argues that an additional ‘regulatory layer’ is added to the traditional bilateral, multilateral and constitutional layers of international law, characterised by bilateral and multilateral treaties, custom and the constitutional treaties of international organisations.<sup>146</sup>

In this setting, risk regulation standards developed on a global level through the cooperation of national regulators challenge the conventional structures of international law-making. This is because states are ‘disaggregating’<sup>147</sup> from unitary state action on the global level, to actions of legislative, judicial and executive actors separately, as they cooperate with their corresponding partners in other states. As explained in the previous section, these new actors also require new measures for interaction, as they usually do not have the power to adopt legally binding measures under international law.<sup>148</sup> The shift of regulatory power to the global level has thus led some scholars to argue for the existence of a ‘global administrative space’, in which tasks like risk regulation, traditionally exercised by national administrative bodies, are now moved to the global level. Here, there is a complex interaction between different institutions on different levels (local, national, regional and global), often in the form of non-binding measures.<sup>149</sup>

#### 4.1.2 The rise of private actors

Next to the increase of regulatory cooperation, also private parties are progressively involved in regulatory decision-making procedures and also act as (self-)regulators.<sup>150</sup> One German scholar speaks of ‘korporative Staatsgewalt’, which can be translated as ‘corporative state authority’, alluding to organised private interest as a new weight in the balance of power of exercising state functions.<sup>151</sup> The rise of private actors has also been discussed in several policy areas on the international level.<sup>152</sup> Fisher for example argues that the involvement of

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<sup>143</sup> S. Cassese, ‘Administrative Law without the State? The Challenge of Global Regulation’, 37(4) *International Law and Politics* (2005), pp. 663-694, p. 681; Ruffert (2012), pp. 1163-1255.

<sup>144</sup> Möllers (2006), p. 327. See also: Möllers (2005a), p. 352ff.

<sup>145</sup> J. Pauwelyn, ‘Informal International Lawmaking: Framing the Concept and Research Questions’, in J. Pauwelyn, R. Wessel & J. Wouters (Eds.), *Informal International Lawmaking* (Oxford: Oxford University Press, 2012), pp. 13-34, p. 19. In the Informal International Lawmaking project, this deviation from the traditional actors in international law is termed ‘actor informality’.

<sup>146</sup> Weiler (2004), p. 549.

<sup>147</sup> A. Slaughter, ‘The Real New World Order’, 76(5) *Foreign Affairs* (1997), pp. 183-197, p. 184.

<sup>148</sup> Section 3.

<sup>149</sup> N. Krisch & B. Kingsbury, ‘Introduction: Global Governance and Global Administrative Law in the International Legal Order’, 17(1) *The European Journal of International Law* (2006), pp. 1-13, p. 1.

<sup>150</sup> F. Cafaggi, ‘Rethinking Private Regulation in the European Regulatory Space’, European University Institute Department of Law, EUI Working Papers Law No. 2006/13, (2006), p. 2.

<sup>151</sup> H. Derderer, *Korporative Staatsgewalt – Integration Privat Organisierter Interessen in die Ausübung von Staatsfunktionen. Zugleich eine Rekonstruktion der Legitimationsdogmatik* (Tübingen: Mohr Siebeck, 2004).

<sup>152</sup> See: C. Cutler, V. Haufler & T. Porter (Eds.), *Private Authority and International Affairs* (Albany: State University of New York Press, 1995).

private actors in EU environmental law has evolved from occasional cases to ‘a non-negotiable requirement of regulatory action’.<sup>153</sup>

This also holds true with regard to standard-setting. In the EU and on the global level, private bodies like public interest non-governmental organisations (NGOs), businesses and organisations in various forms either participate in public standard-setting processes, or have arisen as a source of standards on their own.<sup>154</sup> Private actors have increasingly established themselves as important participants in standard-setting as they dispose over the required expertise and their participation brings the decision-making closer to the subjects of standards.<sup>155</sup>

Regulation developed by the respective experts, is suggested to efficiently and effectively solve certain problems. Often this expertise is located at the level of the regulatee, like a specific industry sector.<sup>156</sup> Since standards are voluntary measures, in principle their impact is very much dependent on whether or not they represent the current technical and scientific state of the art.<sup>157</sup> Thus, the aim to enhance compliance with the standards can also lead to the involvement of private actors.<sup>158</sup> Overall, in the regulation of science and technology, purely hierarchical regulation through public bodies is decreasing.<sup>159</sup> Rather, ‘(...) the very distinction between governmental and non-governmental has become blurred, since the real decision-making process now continually involves, and combines, public and private actors’.<sup>160</sup>

#### 4.2 *Institutional diversity in the face of regulatory complexity: a typology of global standard-setting bodies*

Where public administrative regulators and private interest bodies have been identified as main actors in the setting of risk regulation standards, the institutional structures in the context of which these actors interact demonstrate a large degree of diversity.<sup>161</sup> Global standard-setting bodies can generally be distinguished into 4 types:

- I) international organisations (Section 4.2.1 below),
- II) transnational regulators networks (Section 4.2.2 below),
- III) private standard-setting bodies (Section 4.3.3 below), and

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<sup>153</sup> E. Fisher, ‘Unpacking the Toolbox: Or Why the Public/Private Divide is Important in EC Environmental Law’, Florida State University College of Law – Public Law and Legal Theory Working Paper No. 35, (August 2001), p. 18.

<sup>154</sup> Schepel (2005); A. Peters, L. Koechlin, T. Förster & G. Fenner Zinkernagel (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009b).

<sup>155</sup> Peters, Koechlin & Fenner Zinkernagel (2009a), p. 3; F. Cafaggi & A. Renda, ‘Public and Private Regulation – Mapping the Labyrinth’, Centre for European Policy Studies, CEPS Working Document No 370, (October 2012).

<sup>156</sup> Cafaggi (2006), p. 5; Cafaggi & Renda (2012), p. 5.

<sup>157</sup> Kerwer (2002), p. 618.

<sup>158</sup> Cafaggi (2006), p. 7.

<sup>159</sup> S. Borrás, ‘Three Tensions in the Governance of Science and Technology’, in D. Levi-Faur (Ed.), *The Oxford Handbook of Governance* (Oxford: Oxford University Press, 2012), pp. 429-440, p. 433.

<sup>160</sup> Shapiro (2001), p. 370.

<sup>161</sup> In the following these institutional structures of global standard-setting are discussed in detail, whereas the examples are drawn from the area of risk regulation as well as other policy areas, in order to provide a comprehensive picture of the global standard-setting landscape.

IV) public-private partnerships (Section 4.2.4 below).<sup>162</sup>

The first two types of bodies, I and II, are of a public nature, as their members are state representatives or representatives of public regulatory authorities. In the case of international organisations, the actors are usually government officials and the organisation is set up by an international treaty. In transnational regulators networks, representatives of regulatory bodies cooperate in informal structures. On the other end of the public-private spectrum, purely private bodies (type III) set up by non-governmental actors such as companies, associations or non-governmental organisations also engage in global standard setting. Finally, standard-setting bodies may be characterised by a collaboration of public and private actors in public-private partnerships (type IV). Such bodies transcend the traditional classification in public or private terms and are established in various forms.

**Table 1: Typology of global standard-setting bodies**

|   | Public/Private        | Legally established  | Degree of formalisation   | Actors  |
|---|-----------------------|--|---|---|
| <b>International Organisation</b>       | Public                | Yes, under international law   | High  | State Representatives                           |
| <b>Transnational Regulators Network</b> | Public                | No, informal cooperation in the form of a network  | Low   | Regulators                                      |
| <b>Private Standard-Setting Body</b>    | Private               | Yes, either as company, association of companies or as other private/ non-governmental organisation under national law   | High  | Private Interest Representatives                |
| <b>Public-Private-Partnership</b>       | Hybrid Public-Private | Depending on organisational format:<br>- can be established under national law, e.g. as foundation<br>- <i>can exceptionally be established under international law, e.g. as international organisation</i><br>- can be informal e.g. in the form of a network | Depending on organisational format:<br>- high, if established under national or international law<br>- low, if organised as network | Regulators and Private Interest Representatives |

#### 4.2.1 International organisations

International organisations find their legal basis in a treaty agreed upon by subjects of international law, namely authorised representatives of a sovereign state or international organisations. This Treaty basis forms their pivotal defining element as international organisations. It can provide them with international legal personality, which enables the

<sup>162</sup> See also: Kerwer (2005), pp. 624ff.; Röhl (2007), p. 321f.; S. Wheatley, 'Democratic Governance beyond the State: The Legitimacy of Non-State Actors as Standard-Setters', in A. Peters, L. Koechlin, T. Förster & G. Fenner Zinkernagel (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009), pp. 215-240, p. 219. For a similar categorization, however, with regard to global regulatory bodies in general: B. Kingsbury & R. Stewart, 'Legitimacy and Accountability in Global Regulatory Governance: The Emerging Global Administrative Law and the Design and Operation of Administrative Tribunals of International Organizations', in K. Papanikolaou & M. Hiskaki (Eds.), *International Administrative Tribunals in a Changing World* (London: Esperia Publications Ltd., 2008), pp. 193-220.

retention of rights and duties subject to international law, such as the right to bring claims or to enter into treaties.<sup>163</sup> Standard-setting can take place in the auspices of traditional international organisations which progressively take over administrative tasks, as well as their more traditional mandate of ‘high politics’.

An example of an international organisation that sets risk regulation standards is the Organisation for Economic Co-operation and Development (OECD), which currently comprises 35 member countries.<sup>164</sup> Through its Environmental Directorate the OECD sets testing guidelines for chemical safety as well as good laboratory practice standards.<sup>165</sup> Since the late 1970s the OECD has developed guidelines for the testing of chemicals through the cooperation of experts from specialised authorities of the member countries.<sup>166</sup> These guidelines also affect chemical regulation in EU, as studies to fulfil the information requirements of the European chemicals regulation REACH<sup>167</sup> should be carried out in accordance with these guidelines, where they are approved by the European Chemicals Agency.<sup>168</sup>

While the OECD is formed by a treaty amongst states,<sup>169</sup> international organisations are also capable of forming separate standard-setting bodies, as is exemplified by the Codex Alimentarius, a subsidiary organ of the Food and Agriculture Organization (FAO) and the World Health Organization (WHO).<sup>170</sup> It was established through resolutions of the FAO

<sup>163</sup> International Court of Justice, *Reparations for Injuries Suffered in the Service of the United Nations Case* (1949) ICJ Reports p. 174, p. 179; M. Dixon, *Textbook on International Law*, 5<sup>th</sup> Edition (Oxford: Oxford University Press, 2005), p. 114; J. Klabbbers, *An Introduction to International Institutional Law*, 2<sup>nd</sup> Edition (Cambridge: Cambridge University Press, 2009), p. 6ff; N. White, *The Law of International Organisations*, 2<sup>nd</sup> Edition (Manchester: Manchester University Press, 2005), p. 1ff.; C. Archer, *International Organizations*, 3<sup>rd</sup> Edition (London/New York: Routledge, 2001), p. 1ff.

<sup>164</sup> For a list of members see: <http://www.oecd.org/about/membersandpartners/>, last accessed: 3 April 2017.

<sup>165</sup> See: OECD, OECD Series on Testing and Assessment Number 1 – Guidance Document for the Development of OECD Guidelines for the Testing of Chemicals (as revised in 2009), ENV/JM/MONO(2006)20/REV1, 5 August 2009. The OECD mandate in this area is based on Arts. 2a), 2d), 3, 5a) and 5b) of the Convention on the Organisation for Economic Co-operation and Development of 14 December 1960. This allows for the sharing of information amongst Members (Art. 3) and the taking of decisions and recommendations (Art. 5a) and b)) to Member to ‘promote the efficient use of their economic resources (Art. 2a), and ‘pursue their efforts to reduce or abolish obstacles to the exchange of goods and services and current payments, and maintain and extend the liberalization of capital movements’ (Art. 2d).

<sup>166</sup> For a detailed account of the process of developing the OECD Chemicals Testing Guidelines see: M. Herberg, ‘Global Governance Networks in Action: The Development of Toxicological Test Methods at the OECD’, in O. Dilling, M. Herberg & G. Winter (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 77-108.

<sup>167</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849.

<sup>168</sup> See also: <http://echa.europa.eu/support/oecd-eu-test-guidelines>, last accessed: 3 April 2017.

<sup>169</sup> OECD, Convention on the Organisation for Economic Co-operation and Development of 14 December 1960.

<sup>170</sup> For more detail on the Codex Alimentarius Commission and its standard-setting activities see: Masson-Matthee (2007); Herwig (2011), pp. 171-212; R. Pereira, ‘Why Would International

Conference in 1961 and of the WHO in 1963.<sup>171</sup> Today, the Codex Alimentarius Commission has 187 member countries and, additionally, the EU as a member organisation.<sup>172</sup> Through its Joint Food Standards Programme it develops the Codex Alimentarius, which is a compilation of food standards related to issues like food safety and quality, labelling or the classification of food.<sup>173</sup> It was already discussed earlier that the Codex standards have become very prominent through reinforcements of the WTO and have also strongly influenced EU food regulation.<sup>174</sup>

Although an international organisation by definition can only have subjects of international law – being states and (other) international organisations – as members, this does not prevent private interest representatives from taking part in the standard-setting process. For example, the OECD leaves room in its standard-setting process for non-state experts to participate in meetings. The OECD has established a broad network of experts, consisting of participants from industry, trade unions as well as environmental and animal welfare NGOs, that provide input for the proposed new Test Guidelines.<sup>175</sup> The Codex Alimentarius Commission has opened its operation to private interests, as it was one of the first organisations to invite international non-governmental organisations (NGOs) as observers to sessions of the Commission and its organs, providing them with the right to speak and to obtain documents.<sup>176</sup> Thus, although international organisations do not facilitate the participation of those with private interests as full members, they increasingly open up the participation of private parties through different channels, and hence leave room for influence by private parties.

#### 4.2.2 Transnational regulators networks

Whereas international organisations have been introduced as the classic format of institutionalisation at a global level, less formalised bodies are gaining increasing importance as fora for international regulatory cooperation. In these cases cooperation is not framed through the founding of traditional international organisations, but rather in the form of an informal network. Regulatory actors take part in their administrative function rather than as representatives of the state.

The network as an organisational format has attracted plenty of scholarly attention in

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Administrative Activity Be Any Less Legitimate? – A Study of the Codex Alimentarius Commission?, in A. von Bogdandy, R. Wolfrum, J. von Bernstorff, P. Dann & M. Goldmann (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 541-571; D. Bevilaqua, 'The Codex Alimentarius Commission and its Influence on European and National Food Policy', 1(1) *European Food and Feed Law Review* (2006), pp. 3-14.

<sup>171</sup> WHO/FAO, Statutes of the Codex Alimentarius Commission (Adopted in 1961 by the 11th Session of the FAO Conference and in 1963 by the 16th Session of the World Health Assembly, Revised in 1966 and 2006), in Codex Alimentarius Commission, Procedural Manual – Twenty-third edition, Rome, 2015, pp. 4-6.

<sup>172</sup> See: <http://www.fao.org/fao-who-codexalimentarius/members-observers/en/>, last accessed: 3 April 2017.

<sup>173</sup> A full list of the Codex Standards can be found at: <http://www.fao.org/fao-who-codexalimentarius/standards/list-of-standards/en/>, last accessed: 3 April 2017.

<sup>174</sup> Section 3.

<sup>175</sup> OECD, OECD Series on Testing and Assessment Number 1 – Guidance Document for the Development of OECD Guidelines for the Testing of Chemicals (as revised in 2009), ENV/JM/MONO(2006)20/REV1, 5 August 2009, p. 24.

<sup>176</sup> Masson-Matthee (2007), p. 27ff.; Livermore (2006), p. 766-801.

political science and especially in the field of international relations,<sup>177</sup> but also increasingly in legal literature.<sup>178</sup> However, what exactly constitutes a network is not uniformly defined. Börzel, establishing a common denominator, defined a network as ‘a set of relatively stable relationships which are of non-hierarchical and interdependent nature linking a variety of actors, who share common interests with regard to a policy, and who exchange resources to pursue these shared interest acknowledging that co-operation is the best way to achieve common goals’.<sup>179</sup> Networks thus are understood to constitute a way in which global interactions can be structured without legal formalisation.

For the institutional structure of global standard-setting, networks formed by regulators form the main focus, as opposed to networks of legislators or the judiciary.<sup>180</sup> Accordingly, with regard to global standards, the focus is on transnational regulators networks.

Transnational regulators networks can be characterised by the following:

- (i) in contrast to traditional international organisations, participating representatives are officials of regulatory bodies working in the area concerned, as opposed to diplomats or high level government representatives;<sup>181</sup> and
- (ii) the relationships between actors are not legally formalised but adhere to a loose, yet frequently recurring interactional format with different degrees of formalisation;<sup>182</sup>
- (iii) the members are equal partners and no formal hierarchy applies;<sup>183</sup>
- (iv) the members share resources to reach a common goal;<sup>184</sup>
- (v) the network does not follow a strict organisational plan, predetermining the institutional structure, but is free to evolve over time, adapting to the needs of the parties.<sup>185</sup>

One example of a transnational regulators network engaged in the setting of global standards is the International Organization of Securities Commissions (IOSCO), which comprises national regulators and develops standards for securities in financial regulation.<sup>186</sup>

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<sup>177</sup> Networks have been subject to scholarly debate since the 1990s with a large amount of literature discussing their prospects; for an introduction see e.g. A. Slaughter, *A New World Order* (Princeton/Oxford: Princeton University Press, 2004); A. Slaughter & D. Zaring, ‘Networking Goes International: An Update’, 2 *Annual Review of Law and Social Science* (2006), pp. 211-229; F. van Waarden, ‘Dimensions and Types of Policy Networks’, 21(1-2) *European Journal of Political Research* (1992), pp. 29-52.

<sup>178</sup> For example: K. Ladeur, ‘Towards a Legal Theory of Supranationality – The Viability of the Network Concept’, 3(1) *European Law Journal* (1997), pp. 3-54; K. Raustiala, ‘The Architecture of International Cooperation: Transgovernmental Networks and the Future of International Law’, 43(1) *Virginia Journal of International Law* (2002-2003), pp. 1-92; C. Möllers, ‘Netzwerk als Kategorien des Organisationsrechts – Zur juristischen Beschreibung dezentraler Steuerung’, in J. Obbeke (Ed.), *Nicht-normative Steuerung in Dezentralen Systemen* (Stuttgart: Franz Steiner Verlag, 2005b), pp. 285-302.

<sup>179</sup> T. Börzel, ‘Organizing Babylon – On the Different Conceptions of Policy Networks’, 76(2) *Public Administration* (1998), pp. 253-273, p. 254.

<sup>180</sup> For a detailed analysis of networks of legislators or the judiciary see: Slaughter (2004).

<sup>181</sup> Slaughter & Zaring (2006), p. 215; Raustiala (2002-2003), p. 4-5; Möllers (2005), p. 290f.

<sup>182</sup> Raustiala (2002-2003), p. 5; Börzel (1998), p. 254.

<sup>183</sup> Börzel (1998), p. 254.

<sup>184</sup> Ibidem; Slaughter (2004), p. 186.

<sup>185</sup> Ladeur (1997), p. 48.

<sup>186</sup> For more detail on IOSCO see: D. Zaring, ‘Informal Procedure, Hard and Soft, in International Administration’, 5(2) *Chicago Journal of International Law* (2005), pp. 547-603; A.

### 4.2.3 Private standard-setting bodies

More and more private bodies exercise tasks on an international level than traditionally would have been attributed to the public sphere.<sup>187</sup> Section 4.1.2. introduced the increasing importance of private actors on the global level. This also has an effect on the institutional landscape of global regulation in general, and the setting of global standards, specifically.

Private standard-setting bodies can be set up by associations of companies, such as the Global Good Agricultural Practices (Global GAP) which is an initiative set up by retailers establishing food safety and production standards.<sup>188</sup> Non-governmental organisations (NGOs) are also active in standard setting as exemplified by the Forest Stewardship Council (FSC), a non-governmental organisation encompassing stakeholders such as the World Wildlife Fund (WWF) or businesses like Tetra Pak, enacting standards for forest management.<sup>189</sup>

The most well-known private source of global standards is the International Organization for Standardization (ISO), which is composed of over 160 national standard-setting organisations<sup>190</sup> working in a wide variety of economic, technical, and scientific fields.<sup>191</sup> The ISO has civil personality as an association under the Swiss Civil Code.<sup>192</sup> ISO is often referred to as a private standard-setting body. However, it consists of various national standards organisations. Much like the DIN (Deutsches Institut für Normung e.V. (Germany)), these are usually private organisations incorporating public as well as private profit and non-profit parties. However, some national bodies are public. Examples of ISO Members of a governmental nature include the Ghana Standards Authority (GSA), the Lebanese Standards Institution (LIBNOR), and the Public Authority for Industry Standards and Industrial Services Affairs (KOWSMD, Kuwait).<sup>193</sup> Overall, the ISO can be qualified as a private standard-setting body, as these public institutions form an exception amidst the overarching majority of private members. However, the following section will introduce

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Newman & D. Zaring, 'Regulatory Networks: Power, Legitimacy, and Compliance', in J. Dunoff & M. Pollack (Eds.), *Interdisciplinary Perspectives of International Law and International Relations – The State of the Art* (Cambridge: Cambridge University Press, 2013), pp. 244-265, p. 256; Slaughter (2004).

<sup>187</sup> For more detail on private standard-setting bodies see: Peters, Koechlin, Förster & Fenner Zinkernagel (2009b); A. Marx, M. Maertens, J. Swinnen & J. Wouters, *Private Standards And Global Governance – Economic, Legal and Political Perspectives* (Cheltenham: Edward Elgar Publishing Ltd., 2012); Schepel (2005); Cafaggi (2006), p. 7.

<sup>188</sup> Hachez & Wouters (2011), p. 677-710; C. Lin, 'Public-Private Regime Interactions in Global Food Safety Governance', 69(2) *Food and Drug Law Journal* (2014a), pp. 143-160. For an in-depth discussion of private food standards see Part III 'Private Food Standards and Global Governance Legal Perspectives' of Marx, Maertens, Swinnen & Wouters (2012), pp. 195-309.

<sup>189</sup> See: E. Meidinger, 'The Administrative Law of Global Private-Public Regulation: the Case of Forestry', 17(1) *European Journal of International Law* (2006), pp. 47-87.

<sup>190</sup> See: <https://www.iso.org/about-us.html>, last accessed: 3 April 2017.

<sup>191</sup> See: Röhl (2007), p. 322ff. For a closer analysis of the legitimacy of ISO standards in the field of nanotechnology see: E. Kica & D. Bowman, 'Transnational Governance Arrangements: Legitimate Alternatives to Regulating Nanotechnology?', 7(1) *NanoEthics* (2013), pp. 69-82.

<sup>192</sup> International Organisation for Standardization, ISO Statutes, 17th Edition, 2013, Art. 18(2).

<sup>193</sup> A detailed description of the particular organizational character of ISO can be found here: E. Shamir-Borer, 'Legitimacy without Authority in Global Standardization Governance: The Case of the International Organization for Standardization (ISO)', in S. Cassese, B. Carotti, L. Casini, E. Cavalieri & E. MacDonald (Eds.), *Global Administrative Law: The Casebook*, 3rd Edition, pp. 162-183, available via: <http://www.irpa.eu/wp-content/uploads/2012/08/The-Casebook-Chapter-1.pdf>, last accessed: 3 April 2017.

public-private partnerships, where the core organisational characteristic is the cooperation of public and private bodies.

#### 4.2.4 Public-private partnerships

The increase in power of non-state actors has led to the participation of private parties in policy and decision-making processes in a multitude of regulatory areas on a global level.<sup>194</sup> Whereas the types of standard-setting bodies introduced above can be clearly characterised as either public or private standard-setting bodies, this separation is blurred where standards arise from the cooperation of public and private actors. Such forms of cooperation between state and non-state actors are subsumed under the term ‘public-private partnership’ (PPP).<sup>195</sup> On the one hand, these bodies are defined through the collaboration between government or administrative actors, and on the other hand, either profit or non-profit private organisations such as undertakings or NGOs. Their characteristic trait is the joint decision-making of public and private actors, which entails the sharing of rights and responsibilities between these actors.<sup>196</sup> PPPs do not correspond to one specific form of legal establishment and occur in various organisational forms, complicating the positioning of the term in traditional legal categories.<sup>197</sup>

With regard to membership, public parties can be either regulatory bodies or representatives of governments. Private members may be open to for-profit organisations or non-profit private interest groups like NGOs. The concerned parties enter into these public-private partnerships as they offer advantages over purely governmental regulation. They are equipped to provide better insights into the practical effects of regulatory measures which are already in the drafting process. This opens up access to more resources, and ensures better compliance with the regulation, due to the early involvement of addressees of the measure.<sup>198</sup> These partnerships have grown to fulfil the administrative and governmental tasks that used to be reserved for state actors.<sup>199</sup>

The term ‘public-private partnership’ is often used in national systems, but also in the European Union for forms of outsourcing or contracting-out public tasks such as the building of infrastructure, or the provision of public service such as the maintenance of prisons.<sup>200</sup> However, these mostly contractual partnerships are only one part of the PPP

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<sup>194</sup> M. Schäferhoff, S. Campe & C. Kaan, ‘Transnational Public-Private Partnerships in International Relations: Making Sense of Concepts, Research Frameworks, and Results’, 11(3) *International Studies Review* (2009), pp. 451-474, p. 452.

<sup>195</sup> For a general overview on public-private partnerships: Börzel & Risse (2007), pp. 195-216; S. Linder & P. Vaillancourt Rosenau, ‘Mapping the Terrain of the Public-Private Partnership’, in P. Vaillancourt Rosenau (Ed.), *Public-Private Policy Partnerships* (Cambridge, MA: MIT Press, 2000), pp. 1-19.

<sup>196</sup> I. Kaul, ‘Exploring the Space between Markets and States: Global Public-Private Partnerships’, in I. Kaul & P. Conceicao (Eds.), *The New Public Finance: Responding to Global Challenges* (Oxford/New York: Oxford University Press, 2006), pp. 219-268, p. 222.

<sup>197</sup> K. Abbott, ‘Public Private Partnership’, in R. Wolfrum (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated February 2008, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.

<sup>198</sup> Cafaggi & Renda (2012).

<sup>199</sup> Schäferhoff, Campe & Kaan (2009), pp. 451-452. See also: Linder & Vaillancourt Rosenau (2000), p. 5.

<sup>200</sup> See in this regard: European Commission, Green Paper on Public-Private Partnerships and Community Law on Public Contracts and Concessions, COM(2004) 374 final. In the literature: P. Craig, *Administrative Law*, 7<sup>th</sup> Edition (London: Thomson Sweet & Maxwell, 2003), p. 119ff.; C. Cutler, ‘The Legitimacy of Private Transnational Governance: Experts and the Transnational

spectrum and are not relevant for this research. Moreover, on the international level, PPP is often used in the context of development aid or the promotion of health policy.<sup>201</sup> Partnerships like the Global Fund to Fight AIDS, Malaria and Tuberculosis, or the Global Alliance for Vaccine Immunization (GAVI Alliance), which promotes global health through supporting the research and development of pharmaceutical products for neglected diseases, or improving access to vaccines, recently also attracted the attention of legal scholars.<sup>202</sup> In the development and global health sector PPPs are often integrated into the structure of an existing international organisation, or might be established as a separate entity in an international organisation.<sup>203</sup> These forms of public-private partnerships are not relevant for the analysis of global standard-setting.

Going beyond these policy promotion tasks, or the distribution of funds, public-private partnerships also increasingly engage in regulatory tasks and specifically in standard-setting.<sup>204</sup> An example in the area of sports law is the World Anti Doping Agency (WADA), set up as a foundation under Swiss law, which encompasses governments and private representatives of the Olympic Movement. It sets standards with regard to prohibited substances and their detection, which in turn influences the laws of its member countries.<sup>205</sup> Another example is the International Labour Organisation (ILO), a UN agency where governments, workers and employers agree on labour standards.<sup>206</sup> The International Labour Organisation has been established as an international organisation, it has a unique feature in the sense that its members are states, but the ILO Constitution establishes the delegates representing the member states are two government representatives as well as one representative each for the workers and the employers in the member state.<sup>207</sup> It should be stressed that this is a very exceptional case of formalised participation of private interests in international organisations since, as explained before, IO's usually do not foresee an institutionalised role of private interest representatives.

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Market for Force', 8(1) *Socio-Economic Review* (2010), pp. 157-185; P. Vaillancourt Rosenau (Ed.), *Public-Private Policy Partnerships* (Cambridge, MA: MIT Press, 2000).

<sup>201</sup> The UN and its sub-organisations especially promote cooperation with private parties, defining public-private partnerships as 'voluntary and collaborative relationships between various parties, both State and non-State, in which all participants agree to work together to achieve a common purpose or undertake a specific task and to share risks, responsibilities and benefits.' In: United Nations, Report of the Secretary-General, Enhanced Cooperation between the United Nations and All Relevant Partners, in Particular the Private Sector, A/60/214, 10 August 2005.

<sup>202</sup> L. Clarke, 'The Exercise of Public Power over Global Health through Public-Private Partnerships and the Question of Responsibility Under International Law', 105 *Proceedings of the Annual Meeting of the American Society of International Law* (2011), pp. 96-100; G. Burci, 'Public/Private Partnerships in the Public Health Sector', 6(2) *International Organizations Law Review* (2009), pp. 359-382; D. Aziz, 'Global Public-Private Partnerships in International Law', 2(2) *Asian Journal of International Law* (2012), pp. 339-374.

<sup>203</sup> G. Burci (2009), p. 366ff.; Aziz (2012), p. 346.

<sup>204</sup> Peters, Koechlin & Fenner Zinkernagel (2009a), p. 2; L. Koechlin & R. Calland, 'Standard Setting at the Cutting Edge: An Evidence-Based Typology for Multi-stakeholder Initiatives', in A. Peters, L. Koechlin, T. Förster & G. Fenner Zinkernagel (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009), pp. 84-112; Kaul (2006), p. 233.

<sup>205</sup> L. Casini, 'Global Hybrid Public-Private Bodies: The World Anti-Doping Agency (WADA)', 6(2) *International Organizations Law Review* (2009), pp. 421-446.

<sup>206</sup> Börzel & Risse (2007), pp. 195-216.

<sup>207</sup> International Labour Organisation, ILO Constitution, available via: [http://www.ilo.org/dyn/normlex/en/f?p=1000:62:0::NO:62:P62\\_LIST\\_ENTRIE\\_ID:2453907:NO](http://www.ilo.org/dyn/normlex/en/f?p=1000:62:0::NO:62:P62_LIST_ENTRIE_ID:2453907:NO), last accessed: 3 April 2017.

Generally, public-private partnership can take two formats. On the one hand, they can take the form of an actual institutionalised integration of both public and private actors in an organisation legally established either in national or international law. On the other hand, they can be a cooperative process where public and private actors collaborate but do not form a legally established organization. This means that in order to identify a public-private partnership, one has to look beyond the legal establishment of a body and identify whether it is characterised by the cooperation of public and private actors.

Thus, even where a body is established as a private foundation under national law, it can be a public-private partnership depending on its membership, institutional structure and decision-making process. This is exemplified by the World Anti Doping Agency, which is established as a foundation under Swiss law.<sup>208</sup> Public-private partnerships organised as networks have to be distinguished from the transnational regulators networks on the basis of their membership.<sup>209</sup> Whereas the actors in transnational regulators networks are exclusively public officials, the PPPs that are organised as a network are characterised by the collaboration between public officials and private interest representatives.

This research advocates looking at public-private partnerships as an umbrella term for various forms of hybrid governance, encompassing a variety of legal and de facto organisational forms, which are characterised by the hybrid public-private nature of their membership. The added value of incorporating PPPs as separate in the typology of global standard-setting is that this term manages to grasp the complex interactions that either fall outside the purely public or purely private standard-setting activities, as well as the bodies that are legally established as public or private body. This is through atypical cooperation between public and private within that body do not correspond to the stereotypical public or private characterisation.

### 4.3 *Global standards – governance in action*

The previous analysis introduced an overview of the institutional variety that characterises standard-setting on the global level. It has shown that, first of all, there is a large degree of heterogeneity in the formalisation of standard-setting bodies and the actors which are involved in the standard-setting process. Moreover, it has been shown that the actors and institutions typically characterising international law only account for a part of global standard-setting activities, while in many other cases forms of institutionalisation beyond traditional international law are chosen.

Global standards show several characteristics, distinguishing them from traditional international law. Soft law measures are set through regulatory cooperation, increasingly with the involvement of private interests. These standards deal with technical and scientific matters rather than 'high politics'. Thus, global standard-setting does not easily fit within the legal qualifications that apply to traditional international law, qua subject, object and the actors through which they are set. They are thereby reminiscent of '(global) governance', which works through steering mechanisms originating in the cooperation of administrative authorities, with some degree of involvement of private actors of a voluntary nature.<sup>210</sup> The increasing influence of global standards can thus be seen as epitomising the shift from 'government' to 'governance'.<sup>211</sup> In the social sciences these new forms of international

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<sup>208</sup> Casini (2009), p. 430.

<sup>209</sup> Section 4.2.2.

<sup>210</sup> Tietje (2001), p. 168.

<sup>211</sup> J. Rosenau & E. Czempiel (Eds.), *Governance without Government: Order and Change in World Politics* (Cambridge: Cambridge University Press, 1992); Van Kersbergen & Van Waarden (2004), pp. 143-171; Y. Papadopoulos, 'Shifts in Governance: Problems of Legitimacy and Accountability

interaction are already well theorised under the term ‘global governance’ and also the legal scholarship is paying increasing attention to this phenomenon.

Often used in contrast to government, the term ‘governance’ is synonymous with regulation beyond the formal legal authority of a nation state or a regional organisation like the EU.<sup>212</sup> The move from government to governance is characterised as having made the regulatory processes permeable to the participation of actors other than governments and their administrative counterparts, towards the increasing participation of private stakeholders.<sup>213</sup> A setting in which the term ‘global governance’ has been used to describe the evolution towards de-territorialisation of former state-action towards governance mechanisms in the international sphere.<sup>214</sup>

This changed approach to regulation has been observed internationally,<sup>215</sup> within the EU<sup>216</sup> and also in national contexts.<sup>217</sup> The core idea behind the shift from government to governance is that the complexity and trans-border nature of regulatory objects can no longer be addressed by national government action.<sup>218</sup> New forms of regulatory mechanisms, involving non-hierarchical cooperations of a variety of actors, and non-binding forms of decision-making replace state-centred forms of regulation by binding law.<sup>219</sup> Shifts to standard-setting at a global level leads to the regulation of risk in a ‘polycentric regime’,<sup>220</sup>

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– Synthesising Study of the NOW programme “Shifts in Governance”, Netherlands Organisation for Scientific Research, March 2011, The Hague.

<sup>212</sup> J. Rosenau, ‘Governance, Order and Change in World Politics’, in J. Rosenau & E. Czempiel (Eds.), *Governance without Government: Order and Change in World Politics* (Cambridge: Cambridge University Press, 1992), pp. 1-29, p. 5.

<sup>213</sup> Shapiro (2001), p. 369.

<sup>214</sup> M. Ruffert, ‘Perspektiven des Internationalen Verwaltungsrechts’, in C. Möllers, A. Vosskuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 395-419, p. 403.

<sup>215</sup> Shapiro (2001), pp. 369-377; Rosenau (1992).

<sup>216</sup> See e.g.: Möllers (2006), pp. 313-336; B. Kohler-Koch & R. Eising (Eds.), *The Transformation of Governance in the European Union* (London: Routledge, 1999). In European scholarship the debate has largely taken place in terms of ‘New Governance’. Scott and de Búrca define ‘New Governance’ in the following way: ‘New governance processes generally encourage or involve the participation of affected actors (stakeholders) rather than merely representative actors, and emphasise transparency (openness as a means to information sharing and learning), as well as ongoing evaluation and review. Rather than operating through a hierarchical structure of governmental authority, the ‘centre’ (of a network, a regime, or other governance arrangement) may be charged with ensuring the emergence of the governance infrastructure, and with ensuring coordination or exchange between constituent parts. A further characteristic often present in new governance processes is the voluntary or non-binding nature of the norms.’ G. de Búrca & J. Scott, ‘Introduction: New Governance, Law and Constitutionalism’, in G. de Búrca & J. Scott (Eds.), *Law and New Governance in the EU and the US* (Oxford: Hart Publishing, 2006), pp. 1-12, p. 3. See also: M. Dawson, ‘Three Waves of New Governance in the European Union’, 36(2) *European Law Review* (2011a), pp. 208-225; A. Héretier & M. Rhodes (Eds.), *New Modes of Governance in Europe: Governing in the Shadow of Hierarchy* (Basingstoke/New York: Palgrave Macmillan, 2010); J. Scott & D. Trubek, ‘Mind the Gap: Law and New Approaches to Governance in the European Union’, 8(1) *European Law Journal* (2003), pp. 1-18.

<sup>217</sup> See e.g. J. Kooiman (Ed.), *Modern Governance: New Government – Society Interactions* (London: Sage, 1993); R. Rhodes, *Understanding Governance: Policy Networks, Reflexivity and Accountability* (Buckingham: Open University Press, 1997).

<sup>218</sup> Ruffert (2004), p. 31.

<sup>219</sup> Ruffert (2004), p. 27 and 29.

<sup>220</sup> J. Black, ‘Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes’, 2(2) *Regulation & Governance* (2008), pp. 137-164.

where power is not concentrated in one state but where ‘state and non-state actors are both regulators and regulated’<sup>221</sup> in complex interactions on multiple levels of government and with a variety of actors.

## 5. EUROPEAN REGULATORS AS ACTORS IN THE SETTING OF GLOBAL RISK REGULATION STANDARDS

Previous sections have shown that global standards are incorporated into the EU in its internal market regulation. They have also indicated the complex institutional structures in which standards are set on a global level. To provide a comprehensive picture of the interaction between global standards and risk regulation in the EU, the participation of the EU in such global standard-setting bodies also has to be examined. The following analysis will provide an overview of the legal framework applicable to European bodies and institutions taking part in global standard-setting bodies, with due regard to the institutional landscape of global standard-setting as introduced in the previous section.

Before entering into the analysis, it must be acknowledged that the EU has to be competent to establish external relations. In this respect, it should be mentioned that Article 47 TEU confers international legal personality upon the Union. In general, according to Article 3(5) TEU: ‘(i)n its relations with the wider world, the Union shall uphold and promote its values and interests and contribute to the protection of its citizens (...)’. Article 21(1) TEU provides that the Union ‘shall seek to develop relations and build partnerships with third countries, and international, regional or global organisations’ and ‘promote multilateral solutions to common problems’. Article 220 TFEU provides that ‘appropriate forms of cooperation’ shall be developed with the United Nations and its organs as well as with other international organisations where suitable. However, while these articles are proof of a vision of the EU as a global actor, the legal framework applicable to the EU’s role in global standard-setting is quite fragmented.

### 5.1 *Legal framework for EU participation in global standard-setting bodies*

Concerning the legal framework, it must first be established whether the EU is at all competent to be a member of the global standard-setting bodies. This competence is divided from a vertical perspective, between the EU and its Member States,<sup>222</sup> subject to the limitations set by the principle of conferral.<sup>223</sup> No treaty provision deals explicitly with international standard-setting, so with regard to every specific standard-setting body the Union takes part in, it will have to be established if the EU is competent to engage in external action and in the standard-setting process. In general, competence for external action can be exclusive or shared and can follow explicitly or implicitly from the Treaty provision or from secondary legislation.<sup>224</sup>

Where the EU is competent to regulate certain products or processes in the internal

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<sup>221</sup> Black (2008), p. 137.

<sup>222</sup> In general, besides cases where the European Union has explicit competences to establish external relations – such as the Common Commercial Policy in Art. 207 TFEU or development policy in Art. 211 TFEU – the Union will also be competent to establish relations with international organisations and third states where this follows implicitly from a treaty provision or from secondary legislation.

<sup>223</sup> Art. 5 TEU.

<sup>224</sup> Case 22/70 *Commission v. Council*, ECLI:EU:C:1971:32, concerning a European Road Transport Agreement (ERTA). The *ERTA* doctrine is now codified in Art. 216(1) TFEU and Art. 3(2) TFEU.

market, the internal competences to set risk regulation standards following from the Treaty or secondary legislation can serve as a basis for the implied competence of the EU to participate in international organisations, acting as global standard-setters.<sup>225</sup> With regard to the pharmaceutical standards examined in this thesis, the legal basis for the adoption of European legislation for pharmaceuticals is to be found in the approximation of laws provision, Article 114 TFEU in conjunction with Article 168(4)(c) TFEU. This provision allows for EU legislative action in order to contribute to the achievement of public health objectives through '(m)asures setting high standards of quality and safety for medicinal products and devices for medical use'.<sup>226</sup> Cooperation with international organisations is especially emphasised in Article 168(3) TFEU: the 'Union and the Member States shall foster cooperation with third countries and the competent international organisations in the sphere of public health'.<sup>227</sup> In the protection and improvement of human health the EU can only act in a supporting capacity according to Article 6(a) TFEU. However, the harmonisation of pharmaceutical regulation is based on the shared competence of regulating the internal market (Article 4(2)(a) TFEU), and the shared competence for common safety concerns in public health matters, as provided for in Article 4(2)(k) TFEU.

Given the heterogeneity of global standard-setting bodies, the assessment of the role of the EU in global standard-setting is equally complex. The previous section has established the different types of global standard-setting bodies. In this regard, it has become clear that along with international organisations, the traditional cooperators with states on the global level, other types of bodies also engage in standard-setting. The legal framework that applies to the participation of the EU in these bodies varies.

In the typology of global standards-setting bodies, Section 4.2.1 discussed global standard-setting within international organisations. Once it is established that the EU is competent to be a member of an international organisation it can conclude an accession agreement,<sup>228</sup> pursuant to the procedure established in Article 218 TFEU.<sup>229</sup> It is the competence of the Council to appoint a negotiator, which in the cases concerned in this research, will be the Commission as these standards do not concern CFSP matters.<sup>230</sup> The Council, according to Article 218(5) & (6) TFEU, subsequently decides on authorising the signing of the agreement and adopts a decision concluding the agreement.

Beyond accession to an international organisation, one still has to assess the legal framework that regulates the external representation of the Union within the international

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<sup>225</sup> See also: Eeckhout (2011), p. 122.

<sup>226</sup> Art. 168(4)(c) TFEU.

<sup>227</sup> See also: P. Koutrakos, *EU International Relations Law*, 2<sup>nd</sup> Edition (Oxford/Portland: Hart Publishing, 2015), p. 10.

<sup>228</sup> Opinion 1/76 of the Court of 26 April 1977, Opinion given pursuant to Article 228(1) of the EEC Treaty – 'Draft Agreement establishing a European Laying-up Fund for Inland Waterway Vessels', ECLI:EU:C:1977:63, para. 5. See also: Eeckhout (2011); R. Wessel, 'The Legal Framework for the Participation of the European Union in International Institutions', 33(6) *European Integration* (2011), pp. 621-635. The competence of the Union to become a member of an international organization has to be differentiated from the ability to actually join the organization under international law, which might have restricted membership to states, thereby preventing the Union from becoming a member.

<sup>229</sup> This procedure is exemplified by the Union's accession to the Codex Alimentarius Commission. On 21 December 1993 the Council authorised the Commission to negotiate accession to the Codex. The Commission took the task of negotiating the agreement. In 2003, the Council decided positively on accession to the Codex. See: Council Decision 2003/822/EC of 17 November 2003 on the accession of the European Community to the Codex Alimentarius Commission, OJ L 209, 17 November 2003, pp. 14-21, Preamble (7).

<sup>230</sup> Art. 218(3) TFEU.

organisation, in the sense of who will be entitled to represent the EU and agree to a specific standard in the name of the EU. Based on Article 218 TFEU, the Council has the mandate to externally represent the Union as far as binding international agreements are concerned. For the adoption of these international agreements, the procedure of Article 218 TFEU would again be applicable. Moreover, Article 218(9) TFEU specifies that when a body set up by international agreement adopts acts with legal effects – apart from acts that supplement or amend the institutional framework of the agreement – the Council will adopt a Union position, based on a proposal from the Commission. For the purposes of this research, standards are defined as by definition voluntary measures, which are not legally binding, and fall outside of the scope of Article 218 TFEU.

Here, the *OIV* case indicates that under certain circumstances the procedure of Art. 218(9) TFEU can also apply to standards.<sup>231</sup> This case was concerned with wine standards set by the International Organisation of Vine and Wine (OIV), in which several EU Member States but not the EU itself are members. Central to the dispute was the question of whether the Member States could coordinate their positions within the OIV working groups amongst each other, or whether a Union position had to be established through the procedure of Article 218(9) TFEU, as the OIV standards influenced the *acquis* in this area. The Court came to the conclusion that these standards are ‘capable of decisively influencing the content of the legislation adopted by the EU legislature’.<sup>232</sup> Therefore the Court decided that the OIV standards have legal effect for the purpose of Article 218(9) TFEU. Consequently, their adoption on the global level will require the establishment of a Union position by the Council in accordance with Article 218(9) TFEU.<sup>233</sup> Where standards adopted within an international organisation fall short of producing ‘legal effects’ within the meaning of Article 218(9) TFEU because they are not capable of affecting EU legislation, the specific procedure for international agreements under this article does not apply. This means that the general norm of external representation of the EU has to be relied upon.

Article 17(1) TEU, introduced through the Lisbon Treaty, stipulates that the Commission, ‘(...) shall ensure the Union’s external representation’ except for matters related to ‘the common foreign and security policy, and other cases provided for in the Treaties’. Moreover, Article 220(2) TFEU provides that the Commission, together with the High Representative, implements the EU’s relationships with international organisations. However, the Council is granted policy-making power in Article 16(1) TEU, which also has to be respected on external representation. According to the Commission, the established practice for international non-binding measures which are not politically important – standards which will presumably be qualified as due to their technical and scientific nature – is that the Commission will establish the EU position.<sup>234</sup> It will inform the responsible Council working party in advance and, if required, will conduct a discussion on the topic

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<sup>231</sup> Case C-399/12 *Federal Republic of Germany v. Council of the European Union*, ECLI:EU:C:2014:2258.

<sup>232</sup> Case C-399/12 *Federal Republic of Germany v. Council of the European Union*, ECLI:EU:C:2014:2258, para. 63. Although the recommendations by the International Organisation of Vine and Wine (OIV) are not binding under international law, the EU Regulations applicable to wine in the internal market compared the OIV recommendations to EU law and obliged the Commission to base its decisions on the authorisation of oenological practices on these recommendations, as explained in paragraphs 61-64 of the judgment.

<sup>233</sup> Case C-399/12 *Federal Republic of Germany v. Council of the European Union*, ECLI:EU:C:2014:2258.

<sup>234</sup> European Commission, *Vademecum on the External Action of the European Union*, SEC(2011)881/3, p. 24.

with the working party.<sup>235</sup> Moreover, the Commission will inform the Council working party of the final adopted measures.<sup>236</sup>

Apart from the international organisations as discussed above, standard-setting also takes place in transnational regulators networks or public-private partnerships, as established in Section 4.2.<sup>237</sup> If standard-setting takes place in *fora* that are not formally established in legal terms, which do not require formal accession of its members in the form of international agreements, the procedure established by Article 218 TFEU does not apply.<sup>238</sup> Therefore one has to resort to the general norms for external representation in these cases too.

As established before, these bodies are usually a form of cooperation amongst regulators rather than government representatives as would be the case in traditional international organisations. The internal role of the Commission as the EU's main risk regulator is also reflected externally. In its role as 'core executive'<sup>239</sup> the European Commission not only frames risk regulation on the European level, but is also taking part in global standard-setting bodies. Also where the Commission, as the EU's central administrative risk regulator, is taking part in global standard-setting initiatives, such global administrative activities need to be covered explicitly or implicitly by a legal basis.<sup>240</sup> Thus, for these types of global standard-setting bodies, it is essential to examine the competence of the Commission to take part in global standard-setting bodies.

While the European Commission's role in regulatory cooperation could be based on Article 17(1) TEU, the power of the Commission to externally represent the EU is, however, subject to strict limitations. In *France v. Commission I*, it was determined that the Commission lacks the power to conclude legally binding agreements on behalf of the European Union.<sup>241</sup> Moreover the case *France v. Commission II* clarified that where the Commission concludes guidelines on behalf of the Union, it has to respect the division of powers and the principle of institutional balance – in this case between the Commission and the Council – also in the case of such non-binding measures.<sup>242</sup> According to the principle of institutional balance enshrined in Article 13(2) TEU, the Commission needs to respect the policy-making power granted to the Council under Article 16(1) TEU. Recent case law has also shown that Article 17 TEU does not grant the Commission the power to conclude non-binding agreements on behalf of the European Union, which interfere with the Council's policy making power.<sup>243</sup>

Thus, whether the Commission is competent to participate, on the EU's behalf, in the setting of global standards through informal regulatory cooperation outside of established international organisations, is subject to a case-by-case analysis. Secondary legislation applicable to pharmaceuticals provides the European Commission, together with the European Medicines Agency, with a mandate to establish pharmaceuticals guidelines in the

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<sup>235</sup> Ibidem.

<sup>236</sup> Ibidem.

<sup>237</sup> Private standard setting bodies (Section 4.2.3) are not discussed in this part, since purely private standard-setting bodies per definition do not involve EU regulators.

<sup>238</sup> Case C-233/02 *French Republic v. Commission*, ECLI:EU:C:2004:173, para. 45.

<sup>239</sup> Curtin (2009), p. 64.

<sup>240</sup> E. Schmidt-Aßmann, 'The Internationalization of Administrative Relations as a Challenge for Administrative Law Scholarship', in A. von Bogdandy, R. Wolfrum, J. von Bernstorff, P. Dann & M. Goldmann (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 943-963, p. 953.

<sup>241</sup> Case C-327/91 *French Republic v. Commission*, ECLI:EU:C:1994:305.

<sup>242</sup> Case C-233/02 *French Republic v. Commission*, ECLI:EU:C:2004:173, para. 40.

<sup>243</sup> Case C-660/13 *Council v. Commission*, ECLI:EU:C:2016:616.

Union.<sup>244</sup> As will be addressed later in this thesis, these guidelines, like the global pharmaceutical standards discussed, regulate scientific and technical details with regard to the quality, safety and efficacy of medicinal products. It can thus be argued that cooperation with other regulatory authorities globally is based on this task and does not distort the institutional balance, where the agreed upon global standards do not bind the EU legally.

To conclude, the question of whether the EU can participate in global standard-setting bodies depends on the competence division with the Member States. In the case of international organisations, the accession agreement has to be concluded as prescribed by Article 218 TEU. Where the standards developed in international organisations have legal effect on Union legislation, Article 218(9) TFEU is applicable. Where the standards are, however, set by an international organisation but lack legal effect in the sense of Article 218(9) TFEU, and where standard-setting takes place in informal bodies, the EU can be represented by the Commission, as long as this does not infringe on the policy-making power of the Council enshrined in Article 16(1) TEU.

### 5.2 *European agencies as participants in global standard-setting bodies*

Aside from the European Commission, European agencies also play an increasingly important role in global standard-setting. Established as independent expert bodies in order to provide scientific and technical advice to the Commission,<sup>245</sup> these bodies also act as a support for the European Commission in global standard-setting initiatives. While the agencies generally are not competent to act externally as official EU representatives or to enter into binding commitments in the name of the EU, they often take part in the Union's delegations to international fora as experts.<sup>246</sup> This role of European agencies as actors on the global level is gradually receiving academic attention.<sup>247</sup>

The external dimension of the agencies' work is often induced by their role as sources

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<sup>244</sup> See Chapter 3, Section 4.

<sup>245</sup> For further literature on European agencies and their role in the European Union see: M. Everson, C. Monda & E. Vos (Eds.), *European Agencies In Between Institutions And Member States* (Alphen aan den Rijn: Kluwer Law International, 2014); D. Geradin, R. Muñoz & N. Petit (Eds.), *Regulation Through Agencies in the EU – A New Paradigm of European Governance* (Cheltenham: Edward Elgar, 2006); R. Dehousse, 'Regulation by networks in the European Community: the role of European Agencies', 4(2) *Journal of European Public Policy* (1997), pp. 246-261; E. Chiti, 'The Emergence of a Community Administration: The Case of European Agencies', 37(2) *Common Market Law Review* (2000), pp. 309-343.

<sup>246</sup> European Commission, Vademecum on the External Action of the European Union, SEC(2011)881/3, p. 18f. See opposing view: F. Coman-Kund, *European Union Agencies as Global Actors – A Legal Study of the European Aviation Safety Agency, Frontex and Europol* (Maastricht: Universitaire Pers Maastricht, 2015).

<sup>247</sup> See: Coman-Kund (2015); A. Ott, E. Vos & F. Coman-Kund, 'European Agencies on the Global Scene: EU and International Law Perspectives', in M. Everson, C. Monda & E. Vos (Eds.), *European Agencies In Between Institutions And Member States* (Alphen aan den Rijn: Kluwer Law International, 2014), pp. 87-122; A. Ott, 'EU Regulatory Agencies in EU External Relations: trapped in a Legal Minefield Between European and International Law', 13(4) *European Foreign Affairs Review* (2008), pp. 515-540; M. Groenleer, 'Linking Up Levels of Governance: Agencies of the European Union and International Institutions', in O. Costa & K. Joergensen (Eds.), *The Influence of International Institutions on the European Union: When Multilateralism Hits Brussels* (Basingstoke: Palgrave Macmillan, 2012), pp. 135-154; Groenleer & Gabbi (2013), pp. 479-492; M. Fink, 'Frontex Working Agreements: Legitimacy and Human Rights Concerns Regarding "Technical Relationships"', 28(75) *Utrecht Journal of International and European Law* (2012), pp. 20-35.

of scientific expertise in the Union, which creates an incentive for these bodies to cooperate with their counterparts and other experts all over the world in order to make use of the most up-to-date knowledge and to share resources.<sup>248</sup> The close cooperation with international partners provides them with the opportunity to establish themselves as a ‘hub of regulatory science by providing leadership and catalysing improvements and developments’.<sup>249</sup> Thus regulatory cooperation provides agencies not only with the benefits of resource sharing, but it also forms a route to the consolidation of their expert status vis-à-vis their international counterparts, and also in the EU internally.<sup>250</sup> The external regulatory cooperation activities of agencies can take the form of cooperation activities with agencies of third countries or the participation of agencies in specialised international organisations and bodies, and have to be based on a specific mandate. Such mandates are included in the majority of the founding regulations of the European agencies.<sup>251</sup>

For example, the mandate for the participation of the European Medicines Agency (EMA) in global standard-setting can be deduced from Article 57(1)(j) Regulation 726/2004 describing one of the tasks of the agency as:

[U]pon request, providing technical and scientific support in order to improve cooperation between the Community, its Member States, international organisations and third countries on scientific and technical issues relating to the evaluation of medicinal products, in particular in the context of discussions organised in the framework of international conferences on harmonisation.<sup>252</sup>

Although this provision does not specifically address the mandate of the EMA to participate in the International Council for Harmonisation (ICH), which will be studied in detail later in this thesis,<sup>253</sup> the reference to ‘discussions organised in the framework of international conferences on harmonisation’ can be interpreted to serve as a basis for the EMA involvement in this standard-setting body, which was called the International Conference on Harmonisation until 2015.<sup>254</sup> This Article is introduced by the phrase ‘upon request’, meaning it could point to an occasional ad hoc activity of the EMA, and yet the situation is quite the opposite. In practice, with regard to standard-setting in the ICH, the EMA habitually takes part in the harmonisation process and plays an established and important role in the representation of the EU at the ICH level.<sup>255</sup>

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<sup>248</sup> The European Chemicals Agency (ECHA) for example states in its Work Programme: ‘This external orientation is justified, as the scientific and regulatory issues that the Agency needs to consider as part of its knowledge management are in most cases the same issues that our external partners and stakeholders are facing.’ ECHA, Multi-Annual Work Programme 2014-2018, ECHA-13-A-06.01-EN, September 2013, p. 37.

<sup>249</sup> ECHA, Multi-Annual Work Programme 2014-2018, ECHA-13-A-06.01-EN, September 2013, p. 35.

<sup>250</sup> See: Groenleer (2012), pp. 135-154; Groenleer & Gabbi (2013), pp. 479-492.

<sup>251</sup> Ott, Vos & Coman-Kund, (2014), pp. 87-122. See also: Ott (2008), p. 528; Groenleer & Gabbi (2013), p. 481.

<sup>252</sup> Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 136, 30 April 2004, pp. 1-33, Art. 57(1)(j).

<sup>253</sup> See Chapter 4.

<sup>254</sup> Confirmed in an interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>255</sup> See further Chapter 4; Groenleer & Gabbi (2013), p. 480.

Other European agencies take part in global standard-setting initiatives as well. One example is the European Chemicals Agency (ECHA), which participates in the setting of global chemicals standards and takes part in working groups and task forces of the Organisation for Economic Co-operation and Development (OECD) in support of the Commission.<sup>256</sup> The mandate for the ECHA's activity on the global level can be found in Art. 77 of the REACH Regulation:

'(l) at the Commission's request, providing technical and scientific support for steps to improve cooperation between the Community, its Member States, international organisations and third countries on scientific and technical issues relating to the safety of substances, as well as active participation in technical assistance and capacity building activities on sound management of chemicals in developing countries'.<sup>257</sup>

The work of the European Food Safety Authority (EFSA) also has an external dimension in supporting the Commission in the Codex Alimentarius Commission. Article 23(i) of the General Food Law, which set up the EFSA, provides that one of the tasks of the Authority is:

'(i) to provide scientific and technical assistance, when requested to do so by the Commission, with a view to improving cooperation between the Community, applicant countries, international organisations and third countries, in the fields within its mission'.<sup>258</sup>

Additionally, Article 33 of the General Food Law obliges EFSA to collect data regarding its field of expertise. For this purpose the EFSA should cooperate with organisations in third countries and international organisations.<sup>259</sup> With this legal framework the EFSA has taken an active role in international organisations.<sup>260</sup>

Although the provisions that establish the mandate for external relations of agencies are fairly similar, there is no coherent practice with regard to European agencies participating

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<sup>256</sup> For further information see: <https://echa.europa.eu/about-us/partners-and-networks/international-cooperation/oecd-related-work>, last accessed: 3 April 2017.

<sup>257</sup> Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849, Art. 77.

<sup>258</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24, Art. 23(i).

<sup>259</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24, Art. 33(2).

<sup>260</sup> Groenleer & Gabbi (2013), pp. 479-492. Alongside the Codex, Groenleer and Gabbi point out that the EFSA also supports the Commission in the World Organisation for Animal Health (OIE), the International Plant Protection Convention (IPPC), the European and Mediterranean Plant Protection Organisation (EPPO), the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the World Health Organisation (WHO) and the Food and Agriculture Organisation (FAO).

in global standard-setting. Their role will depend on the *forum* of international cooperation in question. The Commission, the European Parliament and the Council also noted this disparity. In 2012, their Common Approach on decentralised agencies established that the practice of international relations of the European agencies should be more structured.<sup>261</sup> The Common Approach called for the provision of working programmes by the agencies. These should contain planning in their international cooperation and the establishment of working arrangements to coordinate with the Commission Directorate General in charge. The Common Approach also required the approval of the agencies' Management Board for a general international relations strategy, as well as specific initiatives.<sup>262</sup>

Importantly, the Common Approach reconfirmed that agencies need to act within the limits of their mandate and 'are not seen as representing the EU position to an outside audience or as committing the EU to international obligations'.<sup>263</sup> Thus, the role of agencies in regulatory cooperation will be more formalised and structured. This should increase the transparency of the relationship between agencies and the Commission in international regulatory cooperation. It will clarify the impact of the external actions of agencies on the Union's institutional balance as enshrined in Article 13(2) TFEU.<sup>264</sup>

In conclusion, EU agencies have mandates to participate in global standard-setting in their founding regulations, given that they do so at the Commission's request. This means the agencies do not act autonomously in their external cooperation but under the control and in cooperation with the Commission in order to preserve the unity of the EU position.<sup>265</sup> However, apart from the requirement of acting upon request, these mandates are remarkably empty in terms of delimiting the freedom of agency participation in international regulatory cooperation.<sup>266</sup> They neither impose procedural requirements on the agency nor a limit on the subject of cooperation. Thus, although European agencies play a significant role in global regulatory cooperation, this is not extensively regulated in the EU's institutional law. In the future, the growing importance of the agencies in international regulatory cooperation will require further clarification and formalisation in order to guarantee the stability of the Union's institutional balance.

## 6. CONCLUSION

Within the regulation of the internal market, the EU is faced with complex risks, which have led to equally complex regulatory structures addressing them. Global standards have obtained an important role in these regulatory efforts, addressing risk by regulating products and production processes through voluntary expertise-based rules. These standards are primarily addressed to regulators, but the industries that produce the respective products are the second level addressees that ultimately have to apply these standards and are affected by them. However, the voluntary nature of these standards is to some extent misleading.

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<sup>261</sup> European Parliament, Council of the European Union and European Commission, 'Joint Statement of the European Parliament, Council of the EU and European Commission on decentralised agencies', 19 July 2012.

<sup>262</sup> European Parliament, Council of the European Union and European Commission, 'Joint Statement of the European Parliament, Council of the EU and European Commission on decentralised agencies', 19 July 2012, p. 8.

<sup>263</sup> European Parliament, Council of the European Union and European Commission, 'Joint Statement of the European Parliament, Council of the EU and European Commission on decentralised agencies', 19 July 2012, p. 8.

<sup>264</sup> See further: Ott, Vos & Coman-Kund (2014), pp. 87-122.

<sup>265</sup> Groenleer & Gabbi (2013), p. 481.

<sup>266</sup> See also: Ott (2008), p. 531; Mendes (2012), p. 1014.

While there are no legal obligations for the respective regulators to implement these standards into their regulatory framework, global standards can be qualified as soft law. This means that for every standard-setting body and the standards that it adopts, it should not simply be concluded that they are voluntary: a careful analysis as to whether the measures nonetheless create obligations for the parties taking part in standard-setting and affect the legal situation of their addressees, at least indirectly, is required. Global standards are very effective regulatory tools and can become *de facto* binding, in particular because of their basis in horizontal decision-making processes. Some standards have been reinforced through their incorporation into legally binding treaties, or the reference to them in WTO law, creating a presumption of conformity. Where they are implemented, they might become part of legally binding regulation or be used to define legislative requirements. Thus, regardless of their lack of legally binding force, they can introduce certain obligations and have indirect or direct legal effects on individuals.

It was shown that the complex institutional landscape of global standard-setting deviates from traditional international law with regard to the bodies undertaking the standard-setting and the actors involved in them. First of all, with the increase of standards originating in regulatory cooperation, administrators have entered the remit of transnational relations. Where the risks transcend national borders, the regulatory response has to follow suit. Therefore, one can witness the development of a 'global administrative space'<sup>267</sup> in which domestic regulators harmonise their activities. In addition to that, private actors increasingly gain importance as actors on the global level, often due to the specific expertise they can contribute to regulatory processes.

These actors undertake the global setting of standards in different types of bodies, subject to a diverging degree of formalisation. The research distinguished between global standard-setting in international organisations, transnational regulators networks, hybrid transnational regulators networks, purely private bodies and also public-private partnerships. The latter type of bodies transcend the established public and private categorisation and appear in different degrees of formalisation, ranging from the actual institutional integration in a body established by law to (not legally) formalised cooperative processes. Overall, global standards have been qualified as a form of governance characterised by a soft law nature. Their origin is in non-hierarchical regulatory cooperation and the increasing relevance of private actors in the decision-making processes. All of these developments can be brought under the concept of 'governance' as opposed to 'government', in the sense of a renunciation from state-centred top-down enforcement through law.

Such global standards are frequently implemented into the risk regulation framework of the EU either through legislative measures or through the adoption of administrative soft law measure. The EU, especially the Commission and European agencies, actively take part in global standard-setting processes. However, it is also clear that this participation of the Commission and the EU agencies is subject to rules regarding the competence of external representation of the Union, and the principle of institutional balance, which will have to be assessed on a case-by-case basis. Here, especially with regard to European agencies, it was pointed out that although the participation in standard-setting bodies is an important task of the EU administration, EU institutional law still has not established a clear approach to the growing externalisation of EU risk regulation.

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<sup>267</sup> Krisch & Kingsbury (2006), p. 1.

## Chapter 2: Legitimacy of global standards – applying European administrative law

### 1. INTRODUCTION

The previous chapter revealed that regardless of their voluntary character, global standards are followed by the members of standard-setting bodies and are sometimes reinforced through international treaties and/or national law. Although they are soft law, adopted in the form of non-binding recommendations, these atypical forms of regulation – compared to both national and international law – have an important impact on European Union risk regulation.

This impact on EU risk regulation also means that global standards and the processes through which they are developed require in-depth scrutiny. As Zürn has pointed out, ‘the more international institutions intervene in formerly national issues, the more they will be confronted with questions regarding their legitimacy’.<sup>1</sup> Therefore, this chapter will enquire after the legitimacy questions raised by global standard-setting. The transposition of regulatory competences to the transnational level tends to create gaps in the legitimacy of these global structures, a phenomenon that Habermas calls ‘*Legitimitätslücken*’.<sup>2</sup> The fact that standard-setting at a global level is often exercised remotely from public control, and through negotiation between non-elected experts and government officials, generates severe legitimacy concerns in particular.<sup>3</sup>

Hence, this chapter will analyse if and how global standard-setting can be legitimised. It will start with introducing the concept of legitimacy (Section 2). Subsequently, it will address why global standards should be subject to enquiry with regard to how they are legitimised. It will also show that legitimisation through efficiency, as is often brought forward in the justification of standard-setting, is defective in the area of risk regulation (Section 3). The chapter will turn to conceptualising the legitimacy of global standard-setting with a special focus on administrative law on a global level (Section 4) and a European level (Section 5). In this manner, this chapter aims to provide the theoretical framework for the study of pharmaceutical regulation as conducted in the following chapters.

### 2. THE CONCEPT OF LEGITIMACY – AN INTRODUCTION

In essence, when talking about legitimacy one addresses the question of why people follow certain commands or rules. Questioning legitimacy means asking: ‘Why, actually do people obey authority?’<sup>4</sup> Where the legitimacy of a body is assessed, a distinction has to be made between a normative and a socio-empirical approach to determining legitimacy; in the former, whether the exercise of authority should be regarded as legitimate, and in the latter, whether the authority is accepted.<sup>5</sup> Within this distinction, this research focuses on the normative approach.

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<sup>1</sup> M. Zürn, ‘Global Governance and Legitimacy Problems’, 39(2) *Government and Opposition* (2004), pp. 260-287, p. 277.

<sup>2</sup> Habermas (1998), p. 109.

<sup>3</sup> P. Nanz & J. Steffek, ‘Global governance, Participation and the Public Sphere’, 39(2) *Government and Opposition* (2004), pp. 314-335, p. 315; Kerwer (2005), p. 620ff.

<sup>4</sup> S. Kalberg (Ed.), *Max Weber – Readings and Commentary on Modernity* (Malden/Oxford/Carlton: Blackwell, 2005), p. 174.

<sup>5</sup> Zürn (2004), p. 260; Peters, Koechlin & Fenner Zinkernagel (2009a), p. 18f.; Hachez & Wouters (2011), p. 680.

Max Weber conducted a well-established theorization of legitimacy when he inquired the reasons that made people obey commands, at the beginning of the twentieth century, following the deterioration of traditional forms of authority established through religion, monarchy or feudalism.<sup>6</sup> Weber's theory provides for three types of legitimacy: traditional, charismatic and legal-rational.<sup>7</sup> However, in taking a normative approach to legitimacy, one is faced with a variety of factors that have been advocated in the literature to establish whether a certain type of measure constitutes a legitimate exercise of public authority. There is certainly not a unitary perspective on what constitutes legitimacy in the scholarship. Legitimacy has been defined and assessed by many authors in different ways and in relation to different entities.<sup>8</sup> The following section will, therefore, introduce the concept of normative legitimacy and introduce factors that have been argued to legitimate the exercise of authority on the global level.

### 2.1 Normative legitimacy beyond democracy

Democracy is central to legitimising the exercise of authority today, and is thus the starting point of this introduction to normative legitimacy. Especially in a national context, legitimation is connected to the democratic legitimacy of the entity that exercises public authority.<sup>9</sup> Democratic legitimacy operates on the presumption that sovereign people are the sole source of legitimacy.<sup>10</sup> In this regard, democracy is commonly understood as the principle that the will of the people – usually expressed in elections – is reflected in representative bodies which are responsible for decision-making, and, furthermore, that the exercise of public power can only be legitimised if it can be linked to the will of the people.<sup>11</sup>

In this democratic legitimacy context, the legitimacy of international law and international governance was not questioned for a long time, but has become a focal topic for scholars in the past decades.<sup>12</sup> Traditionally legitimacy of international law was argued to

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<sup>6</sup> Kalberg (2005), p. 173.

<sup>7</sup> M. Weber, *Wirtschaft und Gesellschaft – Grundriss der Verstehenden Soziologie*, 5<sup>th</sup> Edition, (Tübingen: Mohr Siebeck, 1972), p. 124; Kalberg (2005), p. 190ff.; G. Poggi, *Weber – A Short Introduction* (Cambridge/Malden: Polity Press, 2008), p. 97f.

<sup>8</sup> See, for an overview of the theoretical works on legitimacy: D. Bodansky, 'Legitimacy in International Law and International Relations', in J. Dunoff & M. Pollack (Eds.), *Interdisciplinary Perspectives on International Law and International Relations – The State of the Art* (Cambridge: Cambridge University Press, 2013), pp. 321-341. For further reading on legitimacy of international bodies see e.g.: I. Hurd, 'Legitimacy and Authority in International Politics', 53(2) *International Organization* (1999), pp. 379-408; R. Keohane, 'Global Governance and Legitimacy', 18(1) *Review of International Political Economy* (2011), pp. 99-109; Livermore (2006), pp. 766-801. For a discussion of EU legitimacy see e.g.: F. Scharpf, *Governing in Europe – Effective and Democratic?* (Oxford: Oxford University Press, 1999); C. Carter & A. Scott, 'Legitimacy and Governance beyond the European Nation State: Conceptualizing Governance in the European Union', 4(4) *European Law Journal* (1998), pp. 429-445.

<sup>9</sup> R. Mayntz, 'Legitimacy and Compliance in Transnational Governance', MPIfG Working Paper 10/5 (2010), p. 8; Weiler (2004), p. 547; Hachez & Wouters (2011), pp. 677-710.

<sup>10</sup> Mayntz (2010), p. 8.

<sup>11</sup> M. Krajewski, 'International Organizations or Institutions, Democratic Legitimacy', in R. Wolfrum (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated May 2008, para. 6, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.

<sup>12</sup> M. Kumm, 'The Legitimacy of International Law: A Constitutionalist Framework of Analysis', 15(5) *European Journal of International Law* (2004), pp. 907-931, p. 907; Bodansky (2013), p. 321.

be based on state consent on the international level.<sup>13</sup> Nowadays, the validity of this argument is largely rejected.<sup>14</sup> Buchanan and Keohane argue that state consent fails as a legitimating factor in global governance for three reasons: (i) not all states are democratic and, thus, lack legitimacy themselves; (ii) where democratic states are consenting, the consent is often not voluntary, due to the pressure they face to participate in important global organisations; (iii) often, state consent itself is not subject to national democratic control.<sup>15</sup> In addition, as the previous chapter has argued, governance on an international level led to an increase in informal measures that do not require formally expressed state consent. This is also due to the growing importance of actors, such as regulators, which are not empowered to consent to legally binding commitments.<sup>16</sup> Thus, state consent is a defective source for democratic legitimacy at the global level.

Undoubtedly, the application of traditional instruments to determine the legitimacy of state power – such as the constitutional principles of a state, legality, constitutional rights, democratic decision-making and control, checks and balances of powers and judicial review – fail to some extent with regard to international governance, as they cannot merely be reproduced outside of the nation state.<sup>17</sup> In search of democracy as a source for the normative legitimacy of the exercise of authority on the global level, one comes to the conclusion that ‘legitimacy of governance beyond the nation-state cannot be but deficient.’<sup>18</sup> This is based on a lack of international *demos* as an essential precondition for democracy.<sup>19</sup> Apart from that, other essential elements of democracy (such as direct elections) are also absent on the global level.<sup>20</sup> Therefore, global governance has been argued to suffer from a ‘democratic deficit’.<sup>21</sup>

Accordingly, the scholarship has moved away from relying on democracy as the exclusive standard of legitimacy to acknowledging different normative factors that can legitimise the exercise of authority on a global level.<sup>22</sup> In order to gain legitimacy these organisations will have to rely on a ‘surrogate political process’, meaning that in order to compensate for the lack of being electorally legitimised they will have to rely on other means to increase their legitimacy, such as accountability and control mechanisms as well as inclusive participation of all relevant stakeholders.<sup>23</sup> According to this view, whether an authority is legitimate may be determined by a variety of ‘source-, procedure- or result-oriented factors or a combination thereof’.<sup>24</sup>

The factors advocated in scholarship to provide bases for legitimacy beyond

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<sup>13</sup> R. Wolfrum, ‘Legitimacy in International Law’, in R. Wolfrum (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated March 2011, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), para. 6, last accessed: 3 April 2017.

<sup>14</sup> Bodansky (2013), p. 330; Weiler (2004), p. 548.

<sup>15</sup> A. Buchanan & R. Keohane, ‘The Legitimacy of Global Governance Institutions’, 20(4) *Ethics and International Affairs* (2006), pp. 405-437, p. 412ff.

<sup>16</sup> Chapter 1, section 3.2 and section 4.1.

<sup>17</sup> Dorbeck-Jung (2008), p. 55; Mayntz (2010), p. 9.

<sup>18</sup> Mayntz (2010), p. 9.

<sup>19</sup> Bodansky (2013), p. 330; Buchanan & Keohane (2006), p. 416.

<sup>20</sup> Mayntz (2010), p. 9; Livermore (2006), p. 780.

<sup>21</sup> R. Dahl, ‘Can International Organizations be Democratic? A Skeptic’s View’, in I. Shapiro & C. Hacker-Cordón (Eds.), *Democracy’s Edges* (Cambridge: Cambridge University Press, 1999), pp. 19-36.

<sup>22</sup> Bodansky (2013), p. 330.

<sup>23</sup> Dorbeck-Jung (2008), p. 55.

<sup>24</sup> Wolfrum (2016).

democracy are diverse, and embrace a multitude of approaches, which sometimes overlap and contradict each other. Bodansky for instance mentions factors such as legality, democratic accountability, expertise or even factors such as tradition or religion, as forming different conceptions of legitimacy within a general concept of legitimacy as the authority to rule.<sup>25</sup> Habermas argued for legitimacy through deliberation.<sup>26</sup> In this approach, the exercise of authority is legitimate when it is based on formalised discourse, enabling the public to express its opinion and contribute to the will-formation.<sup>27</sup> Next to these procedural and substantive factors used to define normative legitimacy beyond democracy, especially in the legal literature, recourse is had to constitutional and administrative law to legitimise authority on the international level.<sup>28</sup>

Another factor considered to constitute legitimacy is the adherence to the rule of law, which essentially consists of three elements: (i) the prevention of the arbitrary exercise of state power, as facilitated by clear and accessible rules that cannot be retroactive; (ii) the principle that law also applies to the state and its institutions, supervised by an independent organ such as the judiciary; and, (iii) non-discriminatory law of general application.<sup>29</sup> Although the rule of law is closely connected to democracy in the sense that in democratic states the rule of law is a constitutive principle,<sup>30</sup> the application of the rule of law to bodies on the international level has also been considered as a mechanism to ensure the legitimacy of such bodies.<sup>31</sup>

Values of good governance – encompassing participation, transparency and accountability, as well as adherence to the rule of law –<sup>32</sup> originated in the development policies in international law, and have arisen as important factors to legitimise global governance. Baldwin and Cave have developed a concept of ‘good regulation’, which promotes five key tests to establish the legitimacy of a regulatory measure or framework.<sup>33</sup> Good regulation requires that the measure is authorised by legislation, in addition to: the existence of appropriate accountability mechanisms, a decision-making procedure that is subject to the standards of fairness, accessibility and openness, as well as sufficient expertise of the regulator, and efficiency of the measure.<sup>34</sup>

It follows that how normative legitimacy of the exercise of power on the global level is defined may vary, taking into account various factors beyond democracy, which differ or overlap according to the legal, political and also moral perspective taken.<sup>35</sup> Apart from the

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<sup>25</sup> Bodansky (2013), p. 324.

<sup>26</sup> Habermas (1996).

<sup>27</sup> Habermas (1996), p. 135.

<sup>28</sup> Bodansky (2013), p. 331.

<sup>29</sup> S. Chesterman, ‘Rule of Law’, in R. Wolfrum (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated July 2007, para. 2, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.

<sup>30</sup> M. Rosenfeld, ‘The Rule of Law and the Legitimacy of Constitutional Democracy’, Cardozo Law School, Public Law Research Paper No. 36, March 2001, available via: <http://ssrn.com/abstract=262350>, last accessed: 3 April 2017.

<sup>31</sup> T. Gemkow & M. Zürn, ‘Constraining International Authority through the Rule of Law Legitimatory Potential and Political Dynamics’, in M. Zürn, A. Nollkaemper & R. Peerboom (Eds.), *Rule of Law Dynamics – In an Era of International and Transnational Governance* (Cambridge: Cambridge University Press, 2012), pp. 68-89.

<sup>32</sup> Chesterman (2016), Article last updated July 2007, para. 20, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.

<sup>33</sup> R. Baldwin & M. Cave, *Understanding Regulation* (Oxford: Oxford University Press, 1999), p. 76-85.

<sup>34</sup> Baldwin & Cave (1999), p. 77.

<sup>35</sup> Bodansky (2013), p. 327.

variety of factors that might form the basis of a legitimate exercise of authority, it is acknowledged that not all factors carry the same weight with regard to different types of exercises of authority, the variety of institutions, and the multiple levels – national, supranational or international – on which they operate.<sup>36</sup> Thus, a ‘differentiated, contextual approach’ is advocated in the literature, which takes into account which type of body exercises authority (for example legislative or judicial), in which context a body is exercising authority (such as environmental law), and the type of authority exercised (hard or soft law).<sup>37</sup> This research is also conducted with the understanding that the assessment of the legitimacy of a body, and its exercise of authority, requires a careful assessment of the context in which the body operates. This entails a normative choice where it places an emphasis on certain legitimacy factors over others.

In the specific case of global standards, the normative question of legitimacy is complex to assess.<sup>38</sup> Governance through global standards constitutes an example of Weiler’s regulatory layer, which in essence forms a system of ‘(g)overnance without government and without the governed – ie. polity’,<sup>39</sup> since a democratic basis for this decision-making as found in the national systems is largely absent. This lack of democratic basis is becoming even more pronounced where this regulatory activity is not established by law, be it national, supranational or international.<sup>40</sup>

Such forms of governance leave the classic separation of power to be found in democratic states, and move to a more complex system of actors and steering mechanisms. With standard-setting, it takes place increasingly on a global level and is not constrained to the territory of sovereign states. When leaving the remit of legally confined national government for the sake of global governance, the mechanisms creating legitimacy of government action available in a national state and international law are also left behind.<sup>41</sup> In governance theory legitimacy is derived from the interaction of public and private interests in decision-making, replacing the democratic legitimacy of state actions.<sup>42</sup> In this regard, a valuable contribution of legal scholarship to the ongoing governance debate is the reassessment of the legitimacy of governance forms, such as standard-setting in a legal context. There is also the question of how the decision-making process should be shaped in order to compensate for the deficit of democratic legitimacy.

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<sup>36</sup> Krajewski (2016), Article last updated May 2008, para. 11, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017; J. Steffek, ‘The Legitimation of International Governance’, 9(2) *European Journal of International Relations* (2003), pp. 249-275, p. 258; Baldwin & Cave (1999), p. 83.

<sup>37</sup> Bodansky (2013), p. 332.

<sup>38</sup> See: Black (2008), p. 149; C. Devaux, ‘The Experts in the Elaboration of the Cape Town Convention: Between Authority and Legitimacy’, 19(6) *European Law Journal* (2013), pp. 843-863, p. 846. On the legitimacy of global governance in general: T. Risse, ‘Transnational Governance and Legitimacy’, in A. Benz & Y. Papadopoulos (Eds.), *Governance and Democracy – Comparing National, European and International Experiences* (Oxon: Routledge, 2006), pp. 179-199; Mayntz (2010); Keohane (2011), pp. 99-109.

<sup>39</sup> Weiler (2004), p. 560.

<sup>40</sup> Black (2008), p. 138.

<sup>41</sup> Livermore (2006), p. 780.

<sup>42</sup> J. Ponce Solé, ‘The History of Legitimate Administration in Europe’, in M. Ruffert (Ed.), *Legitimacy in European Administrative Law: Reform and Reconstruction* (Groningen: European Law Publishing, 2011a), pp. 155-173, p. 161.

## 2.2 *A note on the relationship between legitimacy and accountability*

Accountability, much like legitimacy, does not fit into one fixed definition. It is often intermingled with the legitimacy discussion without clear demarcations between the two concepts.<sup>43</sup> One of the most established definitions of accountability is provided by Bovens. He defined accountability as the relationship between a certain actor and an accountability forum, which is characterised by the obligation of the actor to provide explanations and justifications for its activities. The forum is then entitled to ask for further information and can ultimately pass judgement, which might entail consequences for the actor.<sup>44</sup> This definition of accountability is focused on the ex post accountability of actors, as it is limited to the actor providing an account to the forum after it has acted. This accountability relationship can be established between actors and different types of fora. Therefore, it can be distinguished between political, legal, administrative, professional and social accountability fields.<sup>45</sup>

Some authors treat accountability as an overarching concept which entails the concept of legitimacy. This approach is exemplified by Slaughter, who treats the claim of illegitimacy as one part of the accountability problem of transgovernmental regulatory networks, thereby presenting legitimacy as an element of accountability.<sup>46</sup> However, as has been shown above, other scholars see accountability as an element of legitimacy, thus forming a ‘sub-component’<sup>47</sup> of legitimacy together with other components that can legitimise the exercise of authority. In this latter perspective it is argued that enhancing the accountability of an actor might also positively affect the legitimacy of this actor.<sup>48</sup> However, it is also acknowledged that legitimacy does not necessarily depend exclusively on accountability.<sup>49</sup> It is this approach that will be adhered to in this research, in treating accountability as one component of legitimate regulation.

Where global standard-setting is concerned, one is required to look for accountability mechanisms at the international level. There, the classic electoral accountability understood in the democratic sense – as a relationship between the people and public officials – is bound to be deficient, as was also shown with democracy as legitimacy factor before.<sup>50</sup> Thus with regard to Bovens’ accountability fora, political accountability contributes little to the legitimation of global standard-setting, as there is no electoral accountability on an international level, the control through a directly elected parliament is missing, and, the national parliaments generally only exert a very limited control over the international activities of the executive.<sup>51</sup> This gap in political accountability is matched with a very limited

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<sup>43</sup> Black (2008), p. 149.

<sup>44</sup> M. Bovens, ‘Analysing and Assessing Accountability: A Conceptual Framework’, 13(4) *European Law Journal* (2007), pp. 447-468, p. 450.

<sup>45</sup> M. Bovens, D. Curtin & P. ‘t Hart, ‘Studying the Real World of EU Accountability: Framework and Design’, in M. Bovens, D. Curtin & P. ‘t Hart (Eds.), *The Real World of EU Accountability – What Deficit?* (Oxford: Oxford University Press, 2010), pp. 31-62.

<sup>46</sup> A. Slaughter, ‘Agencies on the Loose? Holding Government Networks Accountable’, in G. Bermann, M. Herdegen & P. Lindseth (Eds.), *Transatlantic Regulatory Cooperation: Legal Problems and Political Prospects* (Oxford: Oxford University Press, 2000), pp. 521-546.

<sup>47</sup> D. Curtin & L. Senden, ‘Public Accountability of Transnational Private Regulation: Chimera or Reality?’, 38(1) *Journal of Law and Society* (2011), pp. 163-188, p. 165.

<sup>48</sup> Papadopoulos (2011), p. 11; E. Fisher, ‘The European Union in the Age of Accountability’, 24(3) *Oxford Journal of Legal Studies* (2004), pp. 495-515, p. 510.

<sup>49</sup> Papadopoulos (2011), p. 11; Black (2008), p. 149.

<sup>50</sup> Section 2.1.

<sup>51</sup> D. Curtin & A. Nollkaemper, ‘Conceptualizing Accountability in International and European Law’, 37 *Netherlands Yearbook of International Law* (2006), pp. 3-20, p. 12.

legal accountability, which is defined as accounting for breaches of obligations established by law through procedures that are also established by law.<sup>52</sup> On the international level legal accountability is mainly limited to state responsibility and state liability,<sup>53</sup> which provide insufficient accountability in the context of global standard-setting. Thus Curtin and Nollkaemper maintain that the shift to governance on the global level has not led to a shift in accountability relationships, compared to accountability relationships in the national states.<sup>54</sup>

However, accountability can also be defined in a broader way, using accountability as an ‘umbrella term’ to cover a variety of concepts such as transparency or responsiveness.<sup>55</sup> Whereas the Bovens definition is limited to *ex post* control, this broader concept of accountability is more concerned with how the rules come into being. It links accountability with the public’s potential to take part in the decision-making process, as well as the transparency of such a process, and furthermore, to a requirement of reason-giving.<sup>56</sup> In this broader sense, accountability encompasses a variety of factors, for which no general consensus exists.<sup>57</sup> In this regard, the broader definition of accountability can then overlap with the definition of legitimacy where factors such as participation, transparency, and reasoned decision-making are deemed constituent of both concepts.

It is this broader definition of accountability that this research will adhere to: it leaves more room to reflect on the various accountability mechanisms on the global level that fall outside Bovens’ narrow definition. In global governance and especially where private actors are involved in standard-setting, the broader definition of accountability reflects the reality of accountability relationships much better at the global level. In their review of accountability of private regulators on the global level, Curtin and Senden advocate a contextual conceptualisation of accountability, that also takes ‘informal, non-traditional and non-governmental accountability mechanisms’ into account.<sup>58</sup> In conclusion, this analysis has presented legitimacy as a concept for establishing the authority of a body to rule, which extends beyond democratic legitimacy. It can be construed through taking different procedural and substantive factors into account, such as transparency or participatory openness, including – but not limited to – the accountability of the body concerned.

### 3. QUESTIONING THE LEGITIMACY OF GLOBAL STANDARD-SETTING

While the previous section introduced the conceptual framework of assessing the legitimacy of an exercise of authority, this section will specifically assess the legitimacy of global standard-setting. It will enquire whether global standards need legitimatisation at all and whether the efficiency of this form of regulation, which is usually claimed as justification for standard-setting on the global level, provides sufficient legitimatisation.

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<sup>52</sup> Curtin & Nollkaemper (2006), p. 11.

<sup>53</sup> Ibidem.

<sup>54</sup> Curtin & Nollkaemper (2006), p. 6.

<sup>55</sup> Bovens (2007), p. 450.

<sup>56</sup> Hachez & Wouters (2011), p. 693.

<sup>57</sup> Curtin & Senden (2011), p. 165.

<sup>58</sup> Curtin & Senden (2011), p. 165 and 179.

### 3.1 Enquiry into the need for the legitimisation of global standards

In principle, legitimacy is associated with justifying the ability to take decisions that are binding and, therefore, employ public authority.<sup>59</sup> Thus in the case of standard-setting, one could ask whether the legitimacy of these rather technical soft law rules should actually be questioned. However, there are several reasons why it is important to analyse the legitimacy of the global standard-setting bodies and the processes they carry out. As established in Chapter 1, although global standards are voluntary measures, in practice these are very effective regulatory measures which are implemented in national/ regional regulatory frameworks, and which the regulated actors adhered to.<sup>60</sup> Thus although these standards are voluntary, based on a case-by-case assessment, they may have the potential to constitute soft law. In terms of legitimation, the non-binding nature behind which global standards might be hidden – avoiding questions of legitimacy – may crumble upon closer assessment.

In this respect, the ‘International Public Authority’<sup>61</sup> scholarship of the Max Planck Institute advocates a broadening of the scope of public international law research, through introducing the concept of ‘the exercise international public authority’. This proposes that ‘any kind of governance activity by international institutions, be it administrative or intergovernmental, should be considered as an exercise of international public authority *if it determines individuals, private associations, enterprises, states, or other public institutions*’.<sup>62</sup> It also does not matter whether the measure in question is legally binding or not.<sup>63</sup> In applying the concept of the exercise of international public authority to global standard-setting, the need for assessing the soft law nature of the standards in question becomes evident. Where these standards are indeed to be qualified as soft law and regulate public or private persons, this form of exercise of public authority also requires legitimisation. Moreover, global standards are not necessarily as technical or purely scientific as they are depicted. Risk regulation and with it global standards often transcend mere questions of technicalities or science, as these matters can contain policy character decisions.<sup>64</sup> Jasanoff explains that ‘regulatory standard-setting involves significant measures of political choice and judgment’.<sup>65</sup>

This can be illustrated by the guidelines of the International Council for Harmonisation (ICH), which will be analysed in detail in this research. The ICH regulates how long and how many people the drugs in question have to be tested on before they can receive marketing authorisation.<sup>66</sup> In this case, the regulators needed to balance the required amount of safety data against faster access to the product, and also considerations of whether this has an impact on the pharmacovigilance systems established for the monitoring

<sup>59</sup> Wolfrum (2016), Article last updated March 2011, para. 1, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.

<sup>60</sup> Chapter 1, section 3.

<sup>61</sup> A. von Bogdandy, R. Wolfrum, J. von Bernstorff, P. Dann & M. Goldmann (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010); M. Goldmann, *Internationale öffentliche Gewalt – Handlungsformen internationaler Institutionen im Zeitalter der Globalisierung* (Heidelberg: Springer, 2015).

<sup>62</sup> von Bogdandy, Dann & Goldmann (2010), p. 5 (emphasis in original).

<sup>63</sup> von Bogdandy, Dann & Goldmann (2010), p. 12.

<sup>64</sup> See: Majone (1984), pp. 15-22; S. Jasanoff, ‘Epistemic Subsidiarity – Coexistence, Cosmopolitanism, Constitutionalism’, 4(2) *European Journal of Risk Regulation* (2013), pp. 133-141; Habermas (1998), p. 165.

<sup>65</sup> Jasanoff (2013), p. 133.

<sup>66</sup> ICH, ICH Harmonised Tripartite Guideline – The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life-Threatening Conditions (E 1), 27 October 1994.

the safety of the product once it is on the market.<sup>67</sup> This requires balancing diverging scientific opinions on when a product is ‘safe (enough)’ and taking decisions with an impact on health care policy. The policy dimension is also exemplified by the ICH guidelines on clinical trials,<sup>68</sup> in which placebo controlled trials are advocated over trials with a control group that receives another comparable medicinal product.<sup>69</sup> This entails an important choice on the definition of the efficacy of a medicinal product: Is it sufficient if the product has a curative effect, or should it be superior to existing treatment? The choice made also has ethical implications with regard to the control group, which receives a placebo instead of an actual cure without knowing. It will entail implications for the health care system in general, as it means that products that are actually inferior to existing ones can be on the market.<sup>70</sup>

Thus, apart from the clarification of technical details, the standard-setting process also has the potential to influence broader policy choices. In particular it is the choices made in situations where science will not resolve the question of what is required for a product to be safe, which compels a standard-setting body to take these decisions.

It is also important to ask these questions of legitimacy with regard to global standards because, as explained in Chapter 1, these standards do address the regulated industry and ultimately affect individuals, especially in the regulated industries.<sup>71</sup> Ultimately consumers are also affected by the quality and safety of products as regulated through standards. As these individuals cannot rely on the protection of their rights through constitutional and administrative national law anymore, questions of legitimacy also become increasingly relevant also for these global governance structures.<sup>72</sup> Where standards (regardless of their voluntary nature) are soft law and constitute an exercise of public authority, assessing their legitimacy becomes imperative, the significance of which is augmented through their potential to contain policy choices.

### 3.2 *Challenging efficiency as a basis for legitimacy of global standards*

The catalysts of global public, private and public-private standard-setting are the globalisation of trade and the increasing complexity and interconnection of risks. The regulatory cooperation of administrative bodies on the global level essentially aims at more regulatory efficiency, while the incorporation of private parties is based on a need for their expertise. Thus, the establishment of global standard-setting bodies as analysed in this research, follows the rhetoric of efficiency and effectiveness in the addressing of global risks.<sup>73</sup> These claims of efficiency are invoked to legitimise global standards, justifying the shift of regulatory decision-making to the global level.

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<sup>67</sup> See: S. Dagon, ‘Global Harmonization through Public-Private Partnership: The Case of Pharmaceuticals’, Istituto di Ricerche sulla Pubblica Amministrazione, Global Administrative Law Working Papers, IRPA GAL Working Paper 2012/2, (2012), p. 14-15.

<sup>68</sup> Most important for the issue discussed: ICH, ICH Harmonised Tripartite Guideline – Choice of Control Group and Related Issues in Clinical Trials (E10), 20 July 2000. See also: ICH, ICH Harmonised Tripartite Guideline – General Considerations for Clinical Trials (E8), 17 July 1997; ICH, ICH Harmonised Tripartite Guideline – Statistical Principles for Clinical Trials (E9), 5 February 1998.

<sup>69</sup> See also: Wallach (2001-2002), p. 861.

<sup>70</sup> Mossialos, Mrazek & Walley (2004), p. 7.

<sup>71</sup> Chapter 1, section 2 and section 3.

<sup>72</sup> Hofmann (2013), p. 435 and 440; Mendes (2012), p. 1015; Möllers (2005a), p. 384.

<sup>73</sup> See: von Bogdandy, Dann & Goldmann (2010), p. 8; S. Quack, ‘Law, Expertise and Legitimacy in Transnational Economic Governance: An Introduction’, 8(1) *Socio-Economic Review* (2010), pp. 3-16; p. 10; Devaux (2013), p. 852ff.; See also: Cutler (2010), pp. 157-185.

Such emphasis on efficiency and its subsequent use as legitimating factor is a very familiar form of argumentation to EU scholars, as has been intensely debated in the analysis of the legitimacy of the EU.<sup>74</sup> Scharpf's distinction between input and output legitimacy, established as general democracy theory in 1975<sup>75</sup> and later applied to the EU,<sup>76</sup> is well known in this regard. As Scharpf's theory addresses the question of legitimacy of entities beyond the national level that cannot rely on democratic legitimacy like a democratic nation state, it also appears to provide a framework for the analysis of the legitimacy of global standard-setting bodies.

According to this theory, input legitimacy refers to 'government by the people' meaning that policy choices reflect the will of the governed.<sup>77</sup> This reflection of the preferences of the governed 'refers to the participatory quality of the process leading to laws and rules as ensured by the "majoritarian" institutions of electoral representation'.<sup>78</sup> Input legitimacy as defined by Scharpf, therefore, looks at legitimacy from the perspective of the democratic basis of an authority. As the name suggests, input legitimacy is part of a theory of how people as a source of democratic power can influence political authority. It includes the participatory openness of a political system, giving those with a broad array of interests access to determine how society is governed.

However, input legitimacy presupposes a 'pre-existing collective identity'<sup>79</sup> of the governed, expressing their will through elections and participatory features. Such a collective identity is based on 'commonalities of history, language, and culture'<sup>80</sup> and, therefore, not existing or even envisaged on the global level. Therefore by its nature, global standard-setting will suffer from a defect in terms of input legitimacy, regardless of whether it might be performed by open and participatory means. In fact, instead of a growing collective identity, the establishment of epistemic communities can be observed on the global level, through building clusters of experts in a certain regulatory sector.<sup>81</sup> According to Möllers this 'sectoralisation' is problematic in terms of input legitimacy. This is because, first of all, it leads to an increased dependency of the administration on its regulated industry. Second of all, it leads to decision-making in a very narrow technical or scientific context, where the greater political, democratic context is disregarded.<sup>82</sup> The regulation of specific sectors becomes decoupled from an open democratic discourse in society.

Looking closely at participatory mechanisms, we may observe that the participation of private parties in global standard-setting is often dominated by industry participation, with other societal interests mostly lacking a prominent role in decision-making on the global

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<sup>74</sup> See e.g.: V. Schmidt, 'Democracy and Legitimacy in the European Union Revisited: Input, Output and "Throughput"', 61(1) *Political Studies* (2013), pp. 2-22; G. Majone, 'Europe's 'Democratic Deficit': The Question of Standards', 4(1) *European Law Journal* (1998), pp. 5-28; A. Moravcsik, 'In Defence of the 'Democratic Deficit': Reassessing Legitimacy in the European Union', 40(4) *Journal of Common Market Studies* (2002), pp. 603-624; A. Menon & S. Weatherill, 'Transnational Legitimacy in a Globalising World: How the European Union Rescues its States', 31(3) *West European Politics* (2008), pp. 397-416.

<sup>75</sup> F. Scharpf, *Demokratietheorie Zwischen Utopie und Anpassung* (Konstanz: Universitätsverlag Konstanz, 1970).

<sup>76</sup> Scharpf (1999).

<sup>77</sup> Scharpf (1999), p. 6.

<sup>78</sup> Schmidt (2013), p. 3.

<sup>79</sup> Scharpf (1999), p. 10.

<sup>80</sup> Bodansky (1999), p. 622f.

<sup>81</sup> On epistemic communities see: P. Haas, 'Introduction: Epistemic Communities and International Policy Coordination', 46(1) *International Organization* (1992), pp. 1-35.

<sup>82</sup> Möllers (2005a), p. 379.

level.<sup>83</sup> An explanation for this phenomenon might be that civil society interests are more diffuse than industry interests and, therefore, more demanding to organise.<sup>84</sup> Additionally, participation in regulatory processes presupposes a high level of expertise, financial as well as in human resources.<sup>85</sup> Thus global standard-setting is often flawed in its input legitimacy due to a lack of common identity of the governed, a removal of decision-making from a democratic to a narrow administrative reasoning, and participatory structures that are unbalanced and do not sufficiently incorporate all stakeholders.

For example, although the ICH is viewed as having broad ‘epistemic legitimacy’ in the sense that the standards are scientifically up to speed, a ‘political legitimacy’ seems to be lacking.<sup>86</sup> This is due to the large influence of industry, in contrast to a lack of representation of patients in the actual decision-making. The Codex Alimentarius Commission is also an interesting example when looking at the input legitimacy of global standard-setting. International non-governmental organisations (NGOs) can be invited as observers to sessions of the Commission, and its organs and committees. It has granted them the right to speak and obtain documents since its establishment in 1963.<sup>87</sup> However, as pointed out by Masson-Matthee, although the measures increasing the inclusiveness of the standard-setting process in the Codex are to be welcomed, problems remain regarding industry dominance within the stakeholders’ granted observer status.<sup>88</sup>

Nevertheless, Scharpf’s argument is that even though input legitimacy is required for a legitimised political system, eventual flaws can be counterbalanced by high output legitimacy.<sup>89</sup> Thus, Scharpf developed another perspective that assessed legitimacy concentrating on the ‘output’ of a political system. Based on the concept of ‘governance for the people’, output legitimacy reviews the legitimacy of an authority based on ‘its capacity to solve problems requiring collective solution’.<sup>90</sup> In contrast to input legitimacy, here the focus is less on a common identity as a basis of authority, but more on a common interest as a yardstick for legitimacy.<sup>91</sup> Output legitimacy essentially refers to the ability to effectively solve a problem in common interest while preventing the abuse of power, which would dilute the achievement of the common interest and render a political system less efficient.<sup>92</sup> Through their problem solving-capacity, decisions then attain *ex post* legitimacy.<sup>93</sup>

When assessing the legitimacy of global standards in Scharpf’s terms the core question will be whether a strong output legitimacy of these standards could justify their lack of democratic basis. When assessing this question one needs to realise ‘the common interest’ that output legitimacy is measured against is not straightforward in standard-setting in the area of risk regulation. Basing the legitimacy of standards on their capacity to solve a problem in the common interest implies that these regulatory decision-making processes have a ‘correct’ outcome, solving the question of risk regulation with a ‘better or worse answer’.<sup>94</sup> However, in risk regulation it is by no means certain that the problems that should

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<sup>83</sup> Mattli (2001), p. 331. See also: A. Kudryavtsev, *Private-Sector Standards as Technical Barriers in International Trade in Goods: In Search of WTO Disciplines* (Oisterwijk: Wolf Legal Publishers, 2015).

<sup>84</sup> Herwig (2011), p. 197.

<sup>85</sup> Ibidem; Dorbeck-Jung (2008), p. 56.

<sup>86</sup> Berman (2011a), p. 55.

<sup>87</sup> Livermore (2006), p. 781f.

<sup>88</sup> Masson-Matthee (2007), p. 275f.

<sup>89</sup> Scharpf (1999), p. 10f.

<sup>90</sup> Scharpf (1999), p. 11.

<sup>91</sup> Ibidem.

<sup>92</sup> Scharpf (1999), p. 13.

<sup>93</sup> Schäferhoff, Campe & Kaan (2009), p. 465.

<sup>94</sup> Bodansky (1999), p. 620.

be addressed by regulation do (only) have one correct solution, as convincingly argued by Majone: '(f)ar from being an almost mechanical process safely relegated to technicians, the setting of health, safety and environmental standards is in reality a microcosm in which conflicting epistemologies, regulatory philosophies, national traditions, social values, and professional attitudes are faithfully reflected'.<sup>95</sup>

Accordingly, standard-setting should not be viewed as a process of applying scientific knowledge, but involves choices regarding the methodology, the approach to risk regulation in general (for example, how risk averse is a regulatory system?),<sup>96</sup> and to a certain degree also 'scientific tradition'.<sup>97</sup> As output legitimacy means that the process in question is devoted to acting in a common interest to guarantee a 'decent standard of living',<sup>98</sup> in a pluralistic society and in the face of complex risks, the administration cannot define the general interest in isolated procedures, but needs to consider different interests.<sup>99</sup> Where only the effectiveness of a regulatory system is considered, the question of legitimacy is placed in the hands of the actors that are powerful enough to determine which outcomes they perceive to efficiently mitigate a certain risk.<sup>100</sup> Therefore, especially in the context of global regulatory standards, a legitimisation solely through the efficiency and output of the process turns into a circular argument.<sup>101</sup> In order to define an effective solution to the regulatory problem and have a legitimate output, input legitimacy is presupposed.<sup>102</sup> In the words of Weiler: 'a legitimacy powerfully skewed to results and away from process, based mostly on outputs and only to a limited degree on inputs, is a weak legitimacy and sometimes none at all'.<sup>103</sup>

Accordingly, the narrative of efficiency and the output legitimacy of global standard-setting do not provide a sufficient basis for its legitimacy. Therefore, the next section will establish a framework for the assessment of legitimacy of global-standard setting beyond the mere output justification, turning to administrative law to provide normative factors that can contribute to the legitimacy of global standard-setting.

#### 4. LEGITIMACY THROUGH ADMINISTRATIVE LAW – ON THE GLOBAL LEVEL?

The previous analysis has shown that democracy-based, input legitimacy is bound to fail in providing a workable framework on the global level. Moreover, the previous section argued that the efficiency of global standard-setting, in terms of output legitimacy, does not provide a convincing basis for the legitimacy of global standard-setting either.

Thus where the introduction to legitimacy in Section 2 of this chapter has advocated a contextual approach to assessing the legitimacy of a body, with regard to standard-setting, it is necessary to look at the role of law, particularly administrative law in the provision of

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<sup>95</sup> Majone (1984), p. 15.

<sup>96</sup> See also: Fisher (2010), p. 7.

<sup>97</sup> Majone (1984), p. 16.

<sup>98</sup> Ponce Solé (2011a), p. 158.

<sup>99</sup> Ponce Solé (2011a), p. 159.

<sup>100</sup> Hachez & Wouters (2011), p. 685.

<sup>101</sup> See: Risse (2006), p. 191f.

<sup>102</sup> Mayntz (2010); p. 11. Mayntz, however, argues that norms for technical appliances or pharmaceuticals do not need democratic legitimation due to their basis in a sound science. (See: Mayntz (2010), p. 12). As argued previously in this research, the author does not agree with this presumption, as science will not always be able to provide a clear answer to the regulatory problems addressed in these standards.

<sup>103</sup> Weiler (2004), p. 562.

legitimacy to global standards.<sup>104</sup> This ensures the legitimacy of the regulatory cooperation of public authorities and the role of private parties in this essentially administrative task. This will be explained in the following.

#### 4.1 *Legal-rational legitimacy through administrative law*

Max Weber's theory of the three types of legitimacy – traditional, charismatic and legal-rational – was alluded to in Section 2.<sup>105</sup> Legal-rational legitimacy is the most relevant for this research, referring to the belief that rules and laws have to be obeyed because 'they have been generated according to norms that authorise certain individuals to issue them, and place various, publicly recognized, constraints on the content commands can take'.<sup>106</sup> In democratic states today the legality of a norm is indeed the basis for its legitimacy.<sup>107</sup>

Thus, Weber's theory of legal-rational legitimacy places an emphasis on how the norms come into being, basing their legitimacy on the fact that they were created through a proper enactment procedure – 'proper' here referring to a whole, socially accepted, system of norms – which leads to the rules being in the common interest and justified. Weber does not address the normative or prescriptive dimension of filling in how a proper procedure looks. Therefore, the legal-rational legitimacy theory does not describe a system of norms that legitimacy can be measured against. In this regard, it does not 'privilege certain social arrangements over other and as such is a "value-free" – concept'.<sup>108</sup>

In democratic states, the function of ensuring the legal-rational legitimacy of administrative actions is based on compliance with the administrative law of the respective legal system.<sup>109</sup> Through accountability of the administration to the legislature in a chain of delegation, administrative law on the national level ensures the democratic legitimacy of administrative action.<sup>110</sup> These administrative actions are legitimised by a legal mandate with powers subject to delimitations, such as through restraining delegation from the legislature to the administration, often through constitutional as well as secondary law, subject to control through judicial review and parliamentary oversight.<sup>111</sup>

Therefore, the administration could rely on the 'transmission belt' of administrative law in order to legitimise its actions.<sup>112</sup> Adhering to this form of legitimation means that 'public administration would be legitimate because of the source of origin of its powers, so far as it limits the execution of the law as approved by the democratic representatives of society'.<sup>113</sup> In this regard, administrative law fulfils essentially three functions: it ensures the proper working of the separation of powers in the institutional structure of a state; it protects the rights of the subjects of administrative decisions; and it contributes to democratic legitimacy through regulating public participation in the decision-making

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<sup>104</sup> See also: Bodansky (2013), p. 330.

<sup>105</sup> Section 2.

<sup>106</sup> Poggi (2008), p. 97.

<sup>107</sup> Mayntz (2010), p. 6.

<sup>108</sup> Steffek (2003), p. 253.

<sup>109</sup> Ponce Solé (2011a), p. 158.

<sup>110</sup> B. Kingsbury, N. Krisch & R. Stewart, 'The Emergence of Global Administrative Law', 68(3&4) *Law and Contemporary Problems* (2005), pp. 15-62, p. 30.

<sup>111</sup> Herwig (2011), p. 189; Fisher (2010), p. 23.

<sup>112</sup> R. Stewart, 'Administrative Law In The Twenty-First Century', 78(2) *New York University Law Review* (2003), pp. 437-460; R. Stewart, 'The Reformation of American Administrative Law', 88(8) *Harvard Law Review* (1975), pp. 1669-1813, p. 1675; Harlow (2013), p. 4; Pereira (2010), p. 565.

<sup>113</sup> Ponce Solé (2011a), p. 158.

process.<sup>114</sup>

Surely, this form of legitimation through adherence to administrative law is not simply transferable to the global level, especially due to a lack of separate legislative, judicial and executive powers. However, in order to contribute to the legitimacy of global standard-setting, administrative law principles applicable to these bodies could make the exercise of administrative functions more accountable, democratic and ensure a protection of the rights of individuals concerned by the decisions. It could give a formalised structure to the regulatory cooperation and could discipline the *ad hoc* development of standard-setting procedures through procedural standards.<sup>115</sup> Indeed, the debate in the European Union surrounding ‘New Governance’ made clear that adherence to principles like participation and transparency as recognised in administrative law will not simply arise in the governance context, but need to be introduced and facilitated through legal mechanisms.<sup>116</sup> In order to provide global governance with a legitimising basis, its framing in administrative law terms is imperative.

One question that still needs to be addressed is whether administrative law will be useful to legitimise international standard-setting where it is carried out by a body that is not of purely public nature, such as the public-private partnerships (PPPs) introduced in Chapter 1.<sup>117</sup> In a traditional Westphalian perspective, on the domestic level, the rule of thumb is that public authority has its origin in the state, enabling institutions to exercise state powers in state capacity.<sup>118</sup> The principles of domestic administrative law are applicable to these bodies exercising state power. On the international level, the distinction between public and private bodies is less clear. Since traditionally, administrative law only applies to public administrative actors as state entities, this would require the development of an administrative law that defines its subjects according to their function, in contrast to their qualification as a state organ.<sup>119</sup>

In this regard, Aman suggests viewing public-private partnerships as an ‘extension of the state’ meaning that they form a new way of exercising state competence.<sup>120</sup> As the tasks carried out by these bodies remain governmental in nature, he argues that public law – or at least the potential for citizens to hold the parties responsible for their actions – should also remain applicable to them.<sup>121</sup> A similar approach is taken by the ‘International Public Authority’ scholarship of the Max Planck Institute, mentioned in Section 3.<sup>122</sup> This argues that public law applies whenever a body carries out a task that is ‘functional equivalent to an activity on a public legal basis’.<sup>123</sup> This research also shares the view that, although certain measures like global standards do not fit into the remit of traditional international law understood as solely regulating state behaviour, because of the impact these global standards have on individuals, they require the attention of the legal scholarship. Given their impact on the individual freedoms and the national democratic processes, they should comply with

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<sup>114</sup> See also: von Bogdandy, Dann & Goldmann (2010), p. 9; Schmidt-Aßmann (2010), p. 947.

<sup>115</sup> Möllers (2005a), p. 384.

<sup>116</sup> Dawson (2011a), p. 220.

<sup>117</sup> See: Chapter 1, section 4.2.4.

<sup>118</sup> M. Goldmann, ‘A Matter of Perspective: Global Governance and the Distinction between Public and Private Authority (and Not Law)’, 5(1) *Global Constitutionalism* (2016), pp. 48-84, p. 74.

<sup>119</sup> Möllers & Terhechte (2011), p. 1441.

<sup>120</sup> A. Aman, ‘The Limits of Globalization and the Future of Administrative Law: Government to Governance’, 8(2) *Indiana Journal of Global Legal Studies* (2001), pp. 379-400, p. 382.

<sup>121</sup> Aman (2001), p. 382 and 398.

<sup>122</sup> Section 3; see in general: von Bogdandy, Wolfrum, von Bernstorff, Dann & Goldmann (2010).

<sup>123</sup> von Bogdandy, Dann & Goldmann (2010), p. 14.

substantive and procedural standards in public law, and in case of global standards specifically administrative law.<sup>124</sup>

The Max Planck scholars stress that their approach goes beyond administrative law principles,<sup>125</sup> and is based on public international law in the broad sense,<sup>126</sup> combining ‘constitutionalization, administrative law perspectives, and international institutional law’.<sup>127</sup> However, it is admitted that ‘the vast majority of the activities under consideration in this project could be considered administrative in a heuristic sense.’ As was discussed in Chapter 1 this research views risk regulation and the setting of regulatory standards as an essentially administrative task and will therefore focus on applying administrative law principles to global standard-setting processes.<sup>128</sup>

Indeed, facing the reality that the essentially public function of developing regulatory standards is no longer an exclusive task of state organs, this research advocates that this should not lead to a deterioration of the protection afforded to individuals by administrative law. In this regard, the procedural protections of administrative law will contribute to the legal-rational legitimacy of the standards produced on a global level. Through the development of administrative norms applicable to these institutions, a legal framework could be developed that would clearly define the currently very complex institutional structures and decision-making processes. Its mechanisms would provide protection to the rights of individuals and contribute to the legitimation of the global standard-setting bodies.<sup>129</sup> Such core principles in a regulatory field where industry interests need to be balanced with the protection of public health are procedural transparency; participatory mechanisms that ensure the incorporation of all concerned interests and the use of independent expertise.<sup>130</sup>

#### 4.2 *Administrative law for global standard-setting bodies*

Following the reasoning above, this research adheres to an approach of filling the gap in norms for legal-rational legitimacy of global governance bodies, with procedural standards derived from administrative law. However, it is a basic principle of law that procedural requirements of a decision-making process are determined in the system where the decision-making takes place. Consequently, as the standard-setting subject to this research takes place on the global level, it needs to be asked whether there are accepted procedural standards for global administrative action, or more specifically for global standard-setting.

In this regard, there is currently no established legal framework applicable to these global governance mechanisms. This creates a situation where although the legitimacy of

<sup>124</sup> See also: M. Ruffert & S. Steinecke, *The Global Administrative Law of Science* (Heidelberg/Dordrecht/London/New York: Springer, 2011), p. 16; P. Dann & M. von Engelhardt, ‘Legal Approaches to Global Governance and Accountability: Informal Lawmaking, International Public Authority, and Global Administrative Law Compared’, in J. Pauwelyn, R. Wessel & J. Wouters (Eds.), *Informal International Law-Making* (Oxford: Oxford University Press, 2012), pp. 106-123, p. 112.

<sup>125</sup> A. von Bogdandy, ‘General Principles of International Public Authority: Sketching a Research Field’, in A. von Bogdandy, R. Wolfrum, J. von Bernstorff, P. Dann & M. Goldmann (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 727-760, p. 738ff; Goldmann (2015), p. 330ff.

<sup>126</sup> von Bogdandy, Dann & Goldmann (2010), p. 16.

<sup>127</sup> Ibidem.

<sup>128</sup> Chapter 1, section 4.1.1.

<sup>129</sup> Ruffert (2007), p. 410.

<sup>130</sup> Röhl (2007), p. 329.

these bodies has been criticised, the gap in the law regulating them creates a legal vacuum, meaning that they are not facing claims of illegality as there simply is no law applying to them.<sup>131</sup> However, in legal scholarship, debates continue on how a legal framework regulating global administrative mbodies could develop.

In his extensive work on the cooperation of administrative bodies on the global level, Tietje points to a very long tradition in German scholarship, arguing for the existence of an international administrative law (*Internationales Verwaltungsrecht*), dating back to the works of Lorenz von Stein in the mid-19th century.<sup>132</sup> Traditionally, international administrative law is characterised as describing the body of law that regulates the collusion of national laws, in situations where administrative activities have a foreign link, serving as public law counterpart to private international law.<sup>133</sup> However, the term ‘international administrative law’ is undergoing a reconceptualisation especially in the German scholarship, being advocated to refer to the administrative law originating on the international level, which encompasses three different bodies of law: the law applicable to administrative institutions on the global level, the international law that has an impact on national administrative legal orders, and, finally, the law that governs the cooperative multilevel administrative processes.<sup>134</sup> International administrative law in this sense should not be understood to form a coherent body of positive law – at least not at the moment – or even a clearly defined scholarship. It should be regarded as a body of law ‘in the making’, both with regard to its practice and the academic debate surrounding it.<sup>135</sup>

A comparable debate has developed in the Global Administrative Law (GAL) scholarship.<sup>136</sup> Global Administrative Law takes the growing interaction of administration on the global level as a starting point, leading to complex interconnected structures of regulatory bodies and informal transnational groups.<sup>137</sup> It is argued by GAL scholarship that democratic legitimacy cannot be derived from a state-centred chain of accountability where the global administrative bodies would be accountable to states, whilst the governments in these states are accountable to their voters and subject to judicial review,<sup>138</sup> because the global level forms a distinct ‘global administrative space’.<sup>139</sup> It is recognised that subsequent to the new forms of global administrative bodies, new legitimacy and accountability challenges arise.

Therefore, the GAL project is working towards the identification of ‘mechanisms, principles, practices, and supporting social understandings that promote or otherwise affect the accountability of global administrative bodies, in particular by ensuring they meet adequate standards of transparency, participation, reasoned decision, and legality, and by

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<sup>131</sup> von Bogdandy, Dann & Goldmann (2010), p. 20.

<sup>132</sup> Tietje (2001), p. 50ff.

<sup>133</sup> Ruffert & Steinecke (2011), p. 20; Schmidt-Aßmann (2010), p. 960. The leading literature in this interpretation of international administrative law is: K. Neumeyer, *Internationales Verwaltungsrecht – Vol. IV: Allgemeiner Teil* (Zürich/Leipzig: Verlag für Recht und Gesellschaft, 1936).

<sup>134</sup> Schmidt-Aßmann (2010), p. 960f.

<sup>135</sup> Möllers & Terhechte (2011), p. 1439; Ruffert (2007), pp. 395-419.

<sup>136</sup> See e.g.: Kingsbury, Krisch & Stewart (2005), p. 30; Krisch & Kingsbury (2006), pp. 1-13; B. Kingsbury & L. Casini, ‘Global Administrative Law Dimensions of International Organizations Law’, 6(2) *International Organizations Law Review* (2009), pp. 319-358; S. Cassese (Ed.), *Research Handbook on Global Administrative Law* (Cheltenham: Edward Elgar, 2016).

<sup>137</sup> Kingsbury, Krisch & Stewart (2005), p. 17.

<sup>138</sup> Kingsbury, Krisch & Stewart (2005), p. 26.

<sup>139</sup> Kingsbury, Krisch & Stewart (2005), p. 25ff.

providing effective review of the rules and decisions they make'.<sup>140</sup> Global administrative law is understood to apply to a variety of subjects beyond what is traditionally understood in the national context as administration, as it is argued to also apply to international organisations, institutions and networks as well as hybrid public-private bodies.<sup>141</sup> The scholarship also includes private bodies exercising public governance function and national administrations acting on the international level in administrative measures into their analysis.<sup>142</sup> Moreover, it acknowledges the growing importance and effectiveness of non-binding forms of regulation on the global level.<sup>143</sup>

However, neither 'international administrative law' nor 'global administrative law' currently form an established area of law or could point out a detailed body of norms applicable to administrative bodies on the global level. The GAL scholarship in this regard admits that 'it is unlikely that a definitive and detailed body or rules and principles governing global administration could presently be formulated, even in relation to formal intergovernmental arrangements'.<sup>144</sup> Moreover, even the desirability of such a fixed set of administrative rules applicable to global governance is debated. Indeed, some scholars point out that even a unified, common set of global administrative law is undesirable; that a 'pluralistic' framework of global administrative law with a multitude of normative systems, which interact in constant competition, is a more efficient approach to framing administrative action on the global level.<sup>145</sup> Whether or not one adheres to this pluralist logic, or rather argues for the benefits of a unified administrative law system on the global level,<sup>146</sup> it becomes clear that a major difficulty in enhancing the legitimacy of global governance through a global administrative law, is the question on which basis this law does or should develop.

#### 4.3 *Assessing the legitimacy of global standard-setting bodies through administrative law: a problem of sources*

Scholars of both 'international administrative law' and 'global administrative law' have different approaches to methodology and the question of identifying sources of administrative law on the global level. Whereas international administrative law scholarship operates a strictly legal approach to the subject, global administrative law can be seen as the legal counterpart to global governance theories,<sup>147</sup> and often carries out empirical studies which can borrow from political science methodologies.<sup>148</sup> This also leads to a different focus with regard to how the phenomenon is studied: global administrative law scholarship,

<sup>140</sup> Kingsbury, Krisch & Stewart (2005), p. 17. See also: B. Kingsbury, 'The Administrative Law Frontier in Global Governance', 99 *Proceedings of the Annual Meeting of the American Society of International Law* (2005), pp. 143-153.

<sup>141</sup> Kingsbury, Krisch & Stewart (2005), p. 17; Kingsbury & Casini (2009), p. 319-358.

<sup>142</sup> Kingsbury, Krisch & Stewart (2005), p. 17.

<sup>143</sup> Krisch & Kingsbury (2006), p. 1; Kingsbury (2005), p. 143.

<sup>144</sup> Kingsbury, Krisch & Stewart (2005), p. 31.

<sup>145</sup> See most prominently: N. Krisch, 'The Pluralism of Global Administrative Law', 17(1) *European Journal of International Law* (2006), pp. 247-278. See also: C. Harlow, 'Global Administrative Law: The Quest for Principles and Values', 17(1) *European Journal of International Law* (2006), pp. 187-214, p. 207ff.

<sup>146</sup> For a very good account of the debate between pluralism and constitutionalism see: G. de Búrca, 'The European Court of Justice and the International Legal Order after *Kadi*', 51(1) *Harvard International Law Journal* (2010), pp. 1-49, p. 31ff. For a critique of a pluralist approach to global administrative law see: Herwig (2011), p. 200.

<sup>147</sup> Kingsbury (2005), pp. 143-153. See also: Ruffert (2007), p. 403.

<sup>148</sup> Möllers & Terhechte (2011), p. 1440; Ladeur (2007), pp. 375-394, p. 375.

on the one hand, has a strong focus on identifying overarching administrative procedural principles. International administrative law, on the other hand, is usually concerned with analysing global phenomena in the context of a specific part of administrative law. This is owed to its origin in German scholarship, where the German administrative law operates a distinction between ‘general administrative law’ (*Allgemeines Verwaltungsrecht*) and ‘special administrative law’ (*Besonderes Verwaltungsrecht*), which then concerns a certain task of the administration, like environmental law.<sup>149</sup>

In international administrative law the scholarship thus approaches the question of defining what actually constitutes international administrative law through an analysis of certain reference areas (*Referenzgebiete*),<sup>150</sup> such as environmental law<sup>151</sup> or migration law.<sup>152</sup> Within these reference areas, the research is devoted to identifying the legal consequences of the globalised administrative activity in this specific area of law, taking the national, supranational and international perspective into account.<sup>153</sup> Within this approach lies the conviction that internationalised administrative law needs to be analysed in the context of national law.<sup>154</sup> The approach is, therefore, to look at reference areas and identify emerging international administrative law, as well as its interaction with national administrative law, which will be followed by a comparison of the findings obtained in the reference areas in order to synthesise a common legal framework of international administrative law.<sup>155</sup>

The GAL scholarship approaches the question of sources differently. Kingsbury, Krisch and Stewart identified three mechanisms through which global administrative law is currently formed: i) national mechanisms applied to hold global administrative bodies accountable; ii) measures adopted by global bodies themselves applying to their procedure; and iii) measures adopted by global bodies regulating the domestic implementation of their norms.<sup>156</sup> Through a deductive approach, the project carries out case studies of global governance bodies to identify the emerging principles of a global administrative law.

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<sup>149</sup> Möllers & Terhechte (2011), p. 1439. This distinction is also referred to as the distinction between ‘Allgemeines Verwaltungsrecht’ and ‘Fachverwaltungsrecht’, see: M. Burgi, ‘§18 Rechtsregime’, in W. Hoffmann-Riem, E. Schmidt-Aßmann & A. Voßkuhle (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 1257-1320, p. 1306ff.

<sup>150</sup> Möllers & Terhechte (2011), p. 1443, C. Möllers, ‘Internationales Verwaltungsrecht – Eine Einführung in die Referenzanalyse’, in C. Möllers, A. Voßkuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 1-6, p. 5f.

<sup>151</sup> W. Durner, ‘Internationales Umweltverwaltungsrecht’, in C. Möllers, A. Voßkuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 121-164; M. Rossi, ‘Europäisiertes internationales Umweltverwaltungsrecht’, in C. Möllers, A. Voßkuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 165-180.

<sup>152</sup> J. Bast, ‘Internationalisierung und De-Internationalisierung der Migrationsverwaltung’, in C. Möllers, A. Voßkuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 279-312; N. Krisch, ‘Das Migrationsrecht und die Internationalisierung des Verwaltungsrechts’, in C. Möllers, A. Voßkuhle & C. Walter (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 313-318.

<sup>153</sup> Ruffert (2007), p. 411; Möllers (2007), p. 3f.

<sup>154</sup> Möllers (2007), p. 3.

<sup>155</sup> Schmidt-Aßmann (2010), p. 963; Möllers (2007), p. 5.

<sup>156</sup> Kingsbury, Krisch & Stewart (2005), p. 31f.

The main procedural principles,<sup>157</sup> identified as currently emerging in global administrative practice, following from the case studies conducted within the GAL project, are:

- procedural participation: affected persons should have their view taken into account.<sup>158</sup> This principle can be divided into the right to participate in the formation of norms and the right to be heard.<sup>159</sup> However, it is recognised that these participation rights are only developing in some areas;<sup>160</sup>
- transparency: encompassing both decisional transparency and access to information.<sup>161</sup> This is also defined as ‘a governance of information, including demands for active transparency and access to information, but also demands for confidentiality and privacy, and for legal or political controls on the gathering and use of policy-shaping information’.<sup>162</sup> With regard to transparency, the GAL project points to several attempts to increase the transparency of formal and informal bodies on the international level;<sup>163</sup>
- reasoned decisions: with regard to a requirement to give reasons, in practice this is rather weak.<sup>164</sup> Cassese additionally identifies the ‘right to decisions based upon scientific and testable data’,<sup>165</sup> which could be brought under the right to reasoned decision in the sense of providing a scientifically sound basis;
- review: as containing the right to review either by national authorities, national courts or tribunals at the international level;<sup>166</sup>
- accountability: first, as an overarching concept for all the above principles,<sup>167</sup> but also in a narrower sense as affecting the liability and immunity of international organisations.<sup>168</sup>

The GAL scholarship has made a valuable contribution in providing proof of emerging principles of an administrative law on global level. However, defining a concrete source on how to fill in these emerging principles for global administrative law remains a difficult task. Casini for example argues that GAL has served to map and provide a framework for very complex governance structures, but that its normative claim is delimited by the fact that ‘the global legal space is still too diverse, and GAL principles display too great a variety of features, depending on the sectors where they are applied’.<sup>169</sup>

The GAL scholarship largely refrained from defining the substantive content of global

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<sup>157</sup> The GAL project also developed some emerging substantive principles for administrative decision-making (proportionality, means-ends rationality, avoidance of unnecessarily restrictive means, legitimate expectations), these are, however, not relevant for this research. See: Kingsbury, Krisch & Stewart (2005), p. 26.

<sup>158</sup> Kingsbury, Krisch & Stewart (2005), p. 37.

<sup>159</sup> Cassese (2005), p. 690f.

<sup>160</sup> Kingsbury, Krisch & Stewart (2005), p. 38.

<sup>161</sup> Ibidem.

<sup>162</sup> Kingsbury & Casini (2009), p. 325.

<sup>163</sup> Kingsbury, Krisch & Stewart (2005), p. 38.

<sup>164</sup> Kingsbury, Krisch & Stewart (2005), p. 39.

<sup>165</sup> Cassese (2005), p. 691.

<sup>166</sup> Kingsbury, Krisch & Stewart (2005), p. 39f.

<sup>167</sup> Krisch & Kingsbury (2006), p. 4f.; Kingsbury (2005), p. 143.

<sup>168</sup> Kingsbury & Casini (2009), p. 325.

<sup>169</sup> L. Casini, ‘Beyond drip-painting? Ten years of GAL and the emergence of a global administration’, 13(2) *International Journal of Constitutional Law* (2015), pp. 473-477, p. 477.

administrative law beyond the level of identifying these general principles.<sup>170</sup> Möllers in his review of ten years of GAL therefore criticized the case study approach, arguing that it does not allow for the substantiation of a more general normative claim.<sup>171</sup> Therefore, although the scholarship on the development of a global administrative law is a helpful contribution to the legal debate surrounding the phenomenon of global governance, a myriad of questions remain about its content and potential sources.<sup>172</sup> This has led to the critique especially from international administrative law scholarship that the GAL project does not engage in in-depth legal analysis, but comes closer to the political science discussion on global governance in its methodology.<sup>173</sup>

The GAL scholarship pleads against developing the content of global administrative law based on national administrative law,<sup>174</sup> a dismissal based on several arguments. First of all, it is pointed out that most national administrative laws are based on the delegation of power from the parliament to the administration and a connected chain of accountability.<sup>175</sup> Thus, the transposition of national administrative law to the global level is essentially discarded, due to the fundamental differences in the institutional structure and overall context on the global level.<sup>176</sup> Furthermore, it is argued that national administrative law is usually concerned with binding decisions directed against individuals, which – although a phenomenon also on the rise at the global level – is not always the case for global decisions, which are more often directed to states.<sup>177</sup> Also, it is reasoned that national review mechanisms, with rights to standing for the individual and the participation of individuals in the decisions-making process, are difficult to achieve at the global level.<sup>178</sup> In addition to that, national administrative law systems themselves differ largely in their procedural administrative law standards,<sup>179</sup> which is a core argument against extending the existing national accountability mechanisms to the global activities of national regulators.<sup>180</sup> However, while the general principles of global administrative law are reoccurring in practice and can be argued to form progressively a global administrative law, their manifestation is rather fragmented. They develop in different modes in the respective bodies, making it difficult to form a benchmark for the assessment of a global standard-setting body's legitimacy.

For this research, both the global and international administrative law scholarships provide important insights. They are testimony of an emerging field of law governing the globalisation of administrative action. This might prove to be a route towards establishing a framework for the assessment of the legal-rational legitimacy of global governance. However, it needs to be acknowledged that this field of law is still in the early stages of its

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<sup>170</sup> Kingsbury, Krisch & Stewart (2005), p. 29.

<sup>171</sup> C. Möllers, 'Ten Years of Global Administrative Law', 13(2) *International Journal of Constitutional Law* (2015), pp. 469-472.

<sup>172</sup> Harlow (2006), pp. 187-214; D. Esty, 'Good Governance at the Supranational Scale: Globalizing Administrative Law', 115(7) *Yale Law Journal* (2005-2006), pp. 1490-1562, p. 1561f.

<sup>173</sup> Möllers (2007), p. 3; Möllers & Terhechte (2011), p. 1440.

<sup>174</sup> Kingsbury, Krisch & Stewart (2005), p. 51. However, there are also examples of GAL scholars advocating to take inspiration from domestic law. See prominently: R. Stewart, 'U.S. Administrative Law: A Model For Global Administrative Law?', 68(3&4) *Law and Contemporary Problems* (2005), pp. 63-108.

<sup>175</sup> Kingsbury, Krisch & Stewart (2005), p. 53f.

<sup>176</sup> *Ibidem*.

<sup>177</sup> Kingsbury, Krisch & Stewart (2005), p. 54.

<sup>178</sup> *Ibidem*.

<sup>179</sup> Harlow (2006), p. 208.

<sup>180</sup> Kingsbury, Krisch & Stewart (2005), p. 55f.

development. Moreover, while the GAL school of thought has led to the identification of emerging general principles, the analysis of international administrative law through reference areas allows for more systematic access to the complex world of global governance, in the context of established national administrative law. The GAL scholarship is concerned with mapping the complex governance structures at the global level, it is less concerned about the interaction of these global structures with states and their national administrative law.<sup>181</sup> In the international administrative law contributions, the administrative activity on the global level is always analysed in the context of its interaction with a national administration.<sup>182</sup>

Although it is acknowledged for the purposes of this research that the direct transposition of national administrative law to the global level might not be feasible, it is still important to look at established legal frameworks to find inspiration for the development of global administrative law. Moreover, global administrative activities do find their way back into the national legal system – for example in the implementation of global standards – which means that the analysis of global practices in the context of established legal systems is necessary and valuable.

Some scholars have argued that without taking inspiration from national administrative law, developing international law to address the governance challenges is not practicable.<sup>183</sup> Echoing that, this research argues that inspiration be drawn from European administrative law in order to fill the general principles of an emerging global (or international) administrative law with procedural rules in the next section.<sup>184</sup>

## 5. APPLYING THE PERSPECTIVE OF EUROPEAN ADMINISTRATIVE LAW

Relying on an approach of ‘intradisciplinary exchange in legal studies’,<sup>185</sup> this section will argue that inspiration can be drawn from EU administrative law in order to study international administrative actors, without disregarding the differences between the European Union, which operates as a supranational organisation between international organisations and national states, and the global administrative space.<sup>186</sup>

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<sup>181</sup> This has been pointed out as an a shortcoming by Sabino Cassese, one of the founding fathers of the GAL scholarship: S. Cassese, ‘Global Administrative Law: The State of the Art’, 13(2) *International Journal of Constitutional Law* (2015), pp. 465-468, p. 467.

<sup>182</sup> Möllers (2007), p. 3.

<sup>183</sup> von Bogdandy, Dann & Goldmann (2010), p. 24; Möllers (2005a), p. 385; Schmidt-Aßmann (2010), p. 959.

<sup>184</sup> See also: Möllers & Terhechte (2011), pp. 1437-1452; M. Savino, ‘EU “Procedural” Supranationalism: On Models for Global Administrative Law’, available via: [http://www.law.nyu.edu/sites/default/files/upload\\_documents/gffsavinopaper.pdf](http://www.law.nyu.edu/sites/default/files/upload_documents/gffsavinopaper.pdf), last accessed: 3 April 2017; E. Chiti & B. Mattarella (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer 2011). More generally geared towards the democratisation of international organizations: A. von Bogdandy, ‘The European Lesson for International Democracy – The Significance of Articles 9 to 12 EU Treaty for International Organizations’, 23(2) *European Journal of International Law* (2012), pp. 315-334. See also Lin who applies lessons learned from European Food Safety Authority to the global level: C. Lin, ‘The European Food Safety Authority in Global Food Safety Governance: A Participant, a Benchmark, and a Model’, in A. Alemanno & S. Gabbi (Eds.), *Foundations of EU Food Law and Policy* (Farnham/Burlington: Ashgate, 2014b), pp. 347-362.

<sup>185</sup> von Bogdandy, Dann & Goldman (2010), p. 24.

<sup>186</sup> See: E. Chiti, ‘EU and Global Administrative Organizations’, in E. Chiti & B. Mattarella (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer, 2011c), pp. 13-39.

This is not a claim that the administrative framework in the EU is flawless, but rather that useful practices identified at the EU level might also contribute to the improvement of processes on a global level. It is fully acknowledged that other useful practices can be derived from other administrative law frameworks; in this context, a ‘westernisation’ of administrative law with a global reach should be avoided.<sup>187</sup> However, research like the one at hand can help to develop procedural rules that might lead to a synthesis of best practices for global administrative action.

### 5.1 *European administrative law as inspiration for an emerging global or international administrative law*

Taking EU administrative law as inspiration for an emerging global administrative law<sup>188</sup> allows for parallels with the evolution of EU administrative law, which faced similar problems in establishing its administrative order above the national level and away from classic forms of democratic legitimacy.<sup>189</sup> EU administrative law has also developed with a strong orientation towards general principles.<sup>190</sup> These principles have been developed and defined, especially through jurisprudence, based on the practice in the Member States and policy-specific EU norms.<sup>191</sup> The general principles conceived of in this way have become the core criteria for assessing the actions of the European administration.<sup>192</sup> It also needs to be stressed that where European regulators are bound to certain procedural rules, the fact that they carry out their regulatory activity in a global body rather than internally in the EU does not per se mean that they can sidestep these rules.<sup>193</sup>

Interestingly, the EU seems to have a vision of exporting its own good governance norms too. Article 3(5) TEU provides that the EU shall contribute to ‘the development of international law’. Moreover, in the field of external actions the Treaties specifically mention Article 21 TEU:

‘2. The Union shall define and pursue common policies and actions, and shall work for a high degree of cooperation in all fields of international relations, in order to:

(...)

(h) promote an international system based on stronger multilateral cooperation and good global governance.’

<sup>187</sup> Harlow (2006), pp. 187-214.

<sup>188</sup> In the following, the term global administrative law refers to administrative law on the global level rather than explicitly to the GAL scholarship. It is not an expression of disregard for international law scholarship, but should be seen in the context of the connotations associated with the terms ‘global’, ‘international’ and also ‘transnational’. It is chosen to refer to global administrative law – like the choice to refer to global standards – to express that the scope does not only refer to state action, but also takes hybrid and private actors into account.

<sup>189</sup> See: E. Schmidt-Aßmann, *Das allgemeine Verwaltungsrecht als Ordnungsidee – Grundlagen und Aufgaben der verwaltungsrechtlichen Systembildung*, 2<sup>nd</sup> Edition (Heidelberg: Springer, 2006).

<sup>190</sup> H.-H. Trute, ‘§6 Die demokratische Legitimation der Verwaltung’, in W. Hoffmann-Riem, E. Schmidt-Aßmann & A. Voßkuhle (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 341-435, p. 414ff; Schmidt-Aßmann (2010), p. 959.

<sup>191</sup> H. Hofmann, J. Schneider & J. Ziller, ‘The Research Network on European Administrative Law’s Project on EU Administrative Procedure – Its Concepts, Approaches and Results’, 7(2) *Review of European Administrative Law* (2014), pp. 45-64, p. 47.

<sup>192</sup> Ibidem.

<sup>193</sup> Mendes (2014), p. 396.

In its White Paper on European Governance the European Commission declares that:

‘(t)he Union should seek to apply the principles of good governance to its global responsibilities. It should aim to boost the effectiveness and enforcement powers of international institutions.’<sup>194</sup>

Apart from the possible contribution to establishing procedural rules for administrative action on the global level, another argument for analysing such global administrative activities from a European administrative law perspective is that these global activities work their way through to the EU level, as the implementation of global standards in the EU demonstrates. Where the global measure is received in the EU through implementation, the legitimacy of this can be questioned, as the global administrative body has not been subject to the same procedural rules that would have to be followed in the EU in adopting the measure.<sup>195</sup>

The clash between procedural rules on the global and EU level is exemplified in the *Kadi* case,<sup>196</sup> where the claimant targeted a regulation originating in an UN Security Council Resolution on the basis of the right to property, to a fair hearing and the right to effective judicial review.<sup>197</sup> The Court in that case declared that ‘the obligations imposed by an international agreement cannot have the effect of prejudicing the constitutional principles of the EC Treaty’.<sup>198</sup>

Arguably, the *Kadi* case is very special due to its anti-terrorism context, and as it concerned the protection of fundamental rights rather than procedural administrative law standards. It is clear that the Court in that ruling stressed the autonomy of the EU legal order and the rights this order protects.<sup>199</sup> It set aside the Regulation due to a violation of fundamental rights. However, Mendes convincingly argued that the values of transparency, participation and good governance are enshrined in the Treaty and therefore form part of the constitutional order of the Union, which is used by the Court in its judicial review.<sup>200</sup> Therefore, where the *Kadi* reasoning is applied to the measures implementing global standards in the EU, it could serve as an argument for questioning such measures, where the standard-setting process from which they originate does not conform to administrative law and good governance norms applicable in the EU. As Curtin and Eckes have explained, the Court in *Kadi* made ‘an attempt to stop the executive from hollowing-out the rule of law from above’.<sup>201</sup> Indeed, where the Court is willing to set aside EU rules implementing binding international law in the form of a Security Council Resolution, a similar logic could be applied to measures implementing global standards.

What remains problematic about the approach of applying EU administrative law to global standards – in terms of the development of a global administrative law – is that

<sup>194</sup> European Commission, European Governance – A White Paper, COM(2001) 428 final, OJ 287, 12 October 2001, pp. 1-29, p. 5.

<sup>195</sup> Mendes (2014), p. 372; Röhl (2007), p. 328; Stewart (2005), p. 69.

<sup>196</sup> Joined cases C-402/05 and 415/05P, *Kadi & Al Barakaat International Foundation v. Council & Commission*, ECLI:EU:C:2008:461.

<sup>197</sup> Joined cases C-402 and 415/05P, *Kadi & Al Barakaat International Foundation v. Council & Commission*, ECLI:EU:C:2008:461.

<sup>198</sup> Joined cases C-402 and 415/05P, *Kadi & Al Barakaat International Foundation v. Council & Commission*, ECLI:EU:C:2008:461, para. 285.

<sup>199</sup> de Búrca (2010), p. 5.

<sup>200</sup> Mendes (2012), p. 1010.

<sup>201</sup> D. Curtin & C. Eckes, ‘The *Kadi* Case: Mapping the Boundaries between the Executive and the Judiciary in Europe’, 5(2) *International Organizations Law Review* (2008), p. 369.

different constituencies will simultaneously apply their administrative law to the same global activity. This potentially leads to conflicting approaches to administrative law on the global level. Therefore, the enforcement of national or European administrative law targeting global actions entails the danger of breaking up the idea of one global administrative law into a kaleidoscope of national norms differing from state to state.<sup>202</sup> Where the alternative is to have no formalised procedural constraints at all, as is currently the case, this nonetheless might be the only option for now.

Apart from the purely EU level perspective, a legitimacy review at the EU level could perform a ‘gatekeeper’<sup>203</sup> function as it forms the ‘entrance level’ for standards into European as well as national risk regulation frameworks.<sup>204</sup> Devaux argues that the EU could perform a ‘legitimacy test (...) with which the EU would evaluate whether a transnational norm deserves its support or not’,<sup>205</sup> through an administrative procedure in which the legitimacy of a norm that is to be implemented in the EU is assessed. Core criteria in this assessment could be the application of EU administrative law, which is applicable to comparable instruments on the EU level. Where a global standard fails this assessment based on European procedural standards, it should not be implemented in the EU.

Overall, there are two main strands of the argument of why this research will use procedural standards originating in European administrative law for the legitimacy assessment of global standards. First of all, these norms work through to the European level, dictating a critical assessment of their legitimacy. This is important in order to prevent a deterioration of the administrative law applicable to the EU administrative bodies through the outsourcing of the decision-making to the global level. It is especially relevant since global standards, once they are implemented in the Union, affect individuals considerably. Moreover, such a practice has the potential to contribute to the formation of global administrative law through contributing best practices of other administrative law systems.

## 5.2 *Procedural standards derived from European administrative law*

Having argued for the application of EU administrative law to global standards, it is now time to look closer at the procedural principles that are relevant for standard-setting on the EU level and as argued thereby also on the global level. This section limits itself in choice from the broad array of administrative law provisions, to those which could be applicable to procedural questions related to risk regulation through standard-setting. Discussions on substantive principles – such as for example proportionality – are left aside, as are the principles that apply to the taking of binding decisions directed towards individuals through the administration, as they are not applicable in standard-setting.<sup>206</sup>

EU administrative law is not thoroughly codified. To a large extent it is developed by the Court of Justice’s rulings on general principles.<sup>207</sup> While a uniform EU law on

<sup>202</sup> Kingsbury, Krisch & Stewart (2005), p. 56; Herberg (2011), p. 84.

<sup>203</sup> The term is borrowed from: Scott (2004), pp. 307-354.

<sup>204</sup> Röhl (2007), p. 337.

<sup>205</sup> Devaux (2013), p. 862.

<sup>206</sup> In general the following principles form the core of European administrative law: the rule of law and specifically the margin of appreciation left to the administrative, equality, non-discrimination, proportionality, the protection of legitimate expectations, legal certainty and the right to a fair administrative procedure. J. Schwarze, *EU Administrative Law* (London: Sweet and Maxwell, 2006), p. cxi.

<sup>207</sup> Schwarze (2006), p. cxi; H. Hofmann & A. Türk, ‘An Introduction to EU Administrative Governance’, in H. Hofmann & A. Türk (Eds.), *EU Administrative Governance* (Cheltenham/Northampton: Edward Elgar, 2006), pp. 1-10, p. 2; S. Kadelbach, ‘EU

administrative procedures, advocated for quite some time in literature<sup>208</sup> and by the European Ombudsman,<sup>209</sup> is now also being requested by the European Parliament,<sup>210</sup> the provisions applying to EU action are currently scattered over a large variety of sources, from hard law to soft law provisions and the case law of the Court. A full description of these norms is beyond the scope of this section; here the focus will rather be to provide an introduction to the core norms applicable to standard-setting in the administrative context.<sup>211</sup>

The starting point of assessing administrative actions is Article 1(2) TEU, which states that ‘decisions are taken as openly as possible’ in the EU. Moreover, Article 2 TEU provides that the EU is based – amongst others – on the principles of democracy and the rule of law. These principles apply to all EU institutions, not just the administrative actors, and find further illustration in the provisions of Articles 9 to 12 TEU, the following of which are relevant for administrative action:

- Art. 10(3) TEU: the right of citizens to take part ‘in the democratic life of the Union’, as well as the openness of decisions.
- Art. 11 TEU:
  - the right of citizens as well as representative organisations to express their opinion and enter into discussion regarding all EU action; (para. 1)
  - and the duty of institutions to ‘maintain an open, transparent and regular dialogue’ with these actors (para. 2).
  - Furthermore, it contains an obligation for the Commission to ‘carry out broad consultations with parties concerned in order to ensure that the Union’s actions coherent and transparent’. (para. 3)

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Administrative Law and the Law of the Europeanized Administration’, in C. Joerges & R. Dehousse (Eds.), *Good Governance in Europe’s Integrated Market* (Oxford: Oxford University Press, 2002), pp. 167-206.

<sup>208</sup> Research Network on European Administrative Law (ReNEUAL), ‘Introduction to the ReNEUAL Model Rules/ Book I – General Provisions’, 2014, available via: [http://www.reneual.eu/images/Home/BookI-general\\_provision\\_2014-09-03\\_individualized\\_final.pdf](http://www.reneual.eu/images/Home/BookI-general_provision_2014-09-03_individualized_final.pdf), last accessed: 3 April 2017; Hofmann, Schneider & Ziller (2014), pp. 45-64; P. Craig, ‘A General Law on Administrative Procedure, Legislative Competence and Judicial Competence’, 19(3) *European Public Law* (2013), pp. 503-524; A. Meuwese, Y. Schuurmans & W. Voermans, ‘Towards a European Administrative Procedure Act’, 2(2) *Review of European Administrative Law* (2009), pp. 3-35.

<sup>209</sup> European Ombudsman, *The European Code of Good Administrative Behaviour*, available via: <http://www.ombudsman.europa.eu/en/resources/code.faces#/page/1>, last accessed: 3 April 2017.

<sup>210</sup> European Parliament, *European administrative procedure law*, Resolution of 15 January 2013, 2012/2024 INL, P7\_TA(2013)0004; European Parliament, *A regulation for an open, efficient and independent European Union administration*, Resolution of 9 June 2016, 2016/2610 RSP, P8\_TA(2016)0279.

<sup>211</sup> For a more detailed discussion see for example: F. Bignami, ‘Three Generations of Participation Rights Before the European Commission’, 68(1) *Law and Contemporary Problems* (2004), pp. 61-83; J. Mendes, *Participation in EU Rule-Making – A Rights-Based Approach* (Oxford: Oxford University Press, 2011b); A. Alemanno, ‘Unpacking the Principle of Openness in EU Law: Transparency, Participation and Democracy’, 39(1) *European Law Review* (2014), pp. 72-90.

Thus, the core values of participation and transparency derive from the principle of democracy, combining to form the principle of openness.<sup>212</sup> In this regard, the principle of transparency refers to the right of individuals to obtain documents, but also to an obligation to make documentation more readily available to the public at large.<sup>213</sup> In general, the principles of participation and transparency should be read as a commitment to open up the decision-making process to comprehension and overview by the general public, besides their function of providing rights such as the access to documents for individuals.<sup>214</sup> These general European constitutional principles apply across all policy areas and activities of the European administration.<sup>215</sup>

In the evolution of European administrative law, the increasing emphasis on the various dimensions of openness is clearly linked to the pursuit of legitimacy and democracy.<sup>216</sup> According to the Court, openness ‘enables citizens to participate more closely in the decision-making process and guarantees that the administration enjoys greater legitimacy and is more effective and more accountable to the citizen in a democratic system’.<sup>217</sup> While the presumed contribution to legitimacy of the principle of openness is subject to vivid debate in scholarship,<sup>218</sup> the constitutionalisation of these principles in the Treaties, and their growing use in Court, have been argued to provide a basis for enhancing the democratic legitimacy of the EU. This is of course dependent upon their application in practice, and potentially also in their further shaping through the Court and the legislator.<sup>219</sup>

As well as these values based on the principle of democracy, norms of good governance have contributed to shaping administrative procedures. In 2001, as a response to a lack of trust and interest of European citizens in the actions of the EU – not only in the context of risk regulation – the European Commission published a White Paper on European Governance, addressing the legitimacy challenges it was facing and proposing changes on the basis of the principles of good governance.<sup>220</sup> Relying on the core values of democracy and the rule of law, the Commission identifies five – sometimes overlapping – principles of good governance: ‘openness, participation, accountability, effectiveness and coherence’<sup>221</sup> and proposed several actions to enforce these principles. Good governance norms are also established in the Treaty with Article 15 (1) TFEU: ‘(i)n order to promote good governance and ensure the participation of civil society, the Union’s institutions, bodies, offices and agencies shall conduct their work as openly as possible’. This openness also includes a right to access to documents (Article 15(3) TFEU), which is also to be found in Article 42 of the Charter, and which has been further implemented through the Access to

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<sup>212</sup> Alemanno (2014), p. 81.

<sup>213</sup> Bignami (2004), p. 71; Alemanno (2014), p. 82.

<sup>214</sup> Hofmann, Schneider & Ziller (2014), p. 51.

<sup>215</sup> Hofmann, Schneider & Ziller (2014), p. 46.

<sup>216</sup> Alemanno (2014), pp. 72-90, p. 82f.

<sup>217</sup> Joined cases C-39/05P and C-52/05P, *Kingdom of Sweden and Maurizio Turco v. Council*, ECLI:EU:C:2008:374, para. 45.

<sup>218</sup> See e.g.: D. Curtin & A. Meijer, ‘Does Transparency Strengthen Legitimacy?’, 11(2) *Information Polity* (2006), pp. 109-122; Mendes (2011b); B. Kohler-Koch & C. Quitkat (Eds.), *De-Mystification of Participatory Democracy* (Oxford: Oxford University Press, 2013).

<sup>219</sup> Alemanno (2014), pp. 72-90; D. Curtin, H. Hofmann & J. Mendes, ‘Constitutionalising EU Executive Rule-Making Procedures: A Research Agenda’, 19(1) *European Law Journal* (2013), pp. 1-21.

<sup>220</sup> European Commission, European Governance – A White Paper, COM(2001) 428 final, OJ 287, 12 October 2001, pp. 1-29.

<sup>221</sup> European Commission, European Governance – A White Paper, COM(2001) 428 final, OJ 287, 12 October 2001, pp. 1-29, p. 10.

Documents Regulation.<sup>222</sup>

The setting of global risk regulation standards, as established in Chapter 1, has been classified as a form of administrative rule-making in the form of soft law. Where the procedural standards as set out in the above should serve the assessment of global standards, it is imperative to enquire whether these rules for administrative action also apply to comparable soft law measures within the EU. With regard to the principle of transparency, including access to documents, there is no provision in the treaties that would indicate that it is only applicable to legislative acts.<sup>223</sup> The Access to Documents Regulation also provides for access to documents which are broadly defined as ‘content whatever its medium (written on paper or stored in electronic form or as a sound, visual or audiovisual recording), concerning a matter relating to the policies, activities and decisions falling within the institution's sphere of responsibility.’<sup>224</sup>

Regarding the principle of participation, Article 11 TEU does not provide a limitation to the applicability of the principle concerning soft law.<sup>225</sup> However, with regard to Article 11(3) TEU, the duty to conduct public consultations is limited to the Commission. According to the Commission's consultation guideline, in conjunction with its impact assessment guideline, there is no obligation to do so – although the Commission occasionally carries out consultations for soft law acts.<sup>226</sup> Article 15 TFEU is addressed to ‘the Union's institutions, bodies, offices and agencies’ and provides that these should work as openly as possible to facilitate the participation of civil society; in contrast, the participation provisions of Article 11(1) and (2) TEU only explicitly apply to the institutions and, thus, not to agencies. Therefore, it seems that while Article 15 TFEU imposes an obligation of openness to all EU bodies, the obligation to maintain a dialogue with civil society and the consultation obligations do not apply to all EU bodies. However, Article 11 TEU does connect participation to democracy, which is a founding principle of the Union according to Article 2 TEU.<sup>227</sup> Thus, although no specific duty to facilitate participation in agencies arises from the treaty, the general commitment to democracy in the EU does apply to agencies. In this spirit they should not bar the participation of civil society.

In this regard, secondary legislation introduces consultation obligations that also apply to other actors and types of measures. For example, the General Food Law –which is the founding regulation of the European Food Safety Authority (EFSA) – provides for the

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<sup>222</sup> Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31 May 2001, pp. 43-48.

<sup>223</sup> See also: European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 26f.

<sup>224</sup> Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31 May 2001, pp. 43-8, Art. 3(a).

<sup>225</sup> See also: European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 28ff.

<sup>226</sup> European Commission, Towards a reinforced culture of consultation and dialogue – General principles and minimum standards for consultation of interested parties by the Commission, COM(2002) 704 final, Brussels, 11 December 2002; European Commission, Impact Assessment Guidelines, SEC(2009) 92, Brussels, 15 January 2009, at pp. 18-19. See: European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 29f.

<sup>227</sup> J. Mendes, ‘Participation and the Role of Law After Lisbon: A Legal View on Article 11 TEU’, 48(6) *Common Market Law Review* (2011c), pp. 1849-1878, p. 1853f.

conduct of an ‘open and transparent public consultation, directly or through representative bodies, during the preparation, evaluation and revision of food law, except where the urgency of the matter does not allow it’.<sup>228</sup> This means that both the Commission and EFSA are obliged to execute public consultation procedures in the evaluation and revision through law, regulation and administrative measures.<sup>229</sup> Indeed stakeholder participation in agencies – established as non-majoritarian expert bodies following quite a technocratic logic of being ‘at the expense of democratic legitimacy’<sup>230</sup> – is especially important, is especially important. Some agencies have therefore created advisory *fora* and stakeholder groups,<sup>231</sup> and some have also adopted consultation procedures, which are comparable to the procedure adopted by the Commission.<sup>232</sup>

In the search for administrative law applicable to standard-setting, one has to mention the right to good administration, which is found in Article 41 of the Charter of Fundamental Rights, and therefore has the same legal value as Treaty provisions.<sup>233</sup> Amongst rights that address the protection of individuals in administrative decision-making procedures in which they are concerned, it also contains the duty of administrators to give reasons for their decisions, which is one of the necessary characteristics of a transparent administrative process. Although Article 41 of the Charter is geared towards single-case decision-making, the Court has applied it also in the broader context of non-legislative rule-making, where it has been used as a criterion for the legality review of non-legislative measures.<sup>234</sup>

In the aforementioned provision, the focus of procedural administrative legitimacy is laid on participation and transparency. However, the Treaties also provide in Article 298(1) TFEU that ‘the institutions, bodies, offices and agencies of the Union shall have the support of an open, efficient and independent European administration’. In the same vein, the Court has also contributed to the definition of EU administrative law. The well-known *Pfizer* case is key to understanding the European risk regulation framework.<sup>235</sup> This case established that risks must be assessed by scientific experts consulted on the basis of the ‘principles of excellence, independence and transparency’.<sup>236</sup> While efficiency and excellence are legally difficult to assess in matters of risk regulation,<sup>237</sup> this means that the independence of administrative actors is a core principle in the assessment of legitimacy of administrative action, in addition to transparency and participation, especially in the field of risk regulation. In this respect, independence should be understood both in an inter-institutional sense as

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<sup>228</sup> Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority, and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24, Art. 9.

<sup>229</sup> Mendes (2011a), p. 121.

<sup>230</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 46.

<sup>231</sup> H. Hofmann, G. Rowe & A. Türk, *Administrative Law and Policy of the European Union* (Oxford: Oxford University Press, 2011), p. 305.

<sup>232</sup> Mendes (2011c), p. 1853f.

<sup>233</sup> See: J. Ponce Solé, ‘EU Law, Global Law and the Right to Good Administration’, in E. Chiti & B. Mattarella (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer, 2011b), pp. 133-145.

<sup>234</sup> H. Hofmann & B. Mihaescu, ‘The Relation between the Charter’s Fundamental Rights and the Unwritten General Principles of EU law: Good Administration as the Test Case’, 9(1) *European Constitutional Law Review* (2013), pp. 73-101, p. 87. See for example: Joined cases C-154/04 and C-155/04 *Alliance for Natural Health*, ECLI:EU:C:2005:449, para. 82.

<sup>235</sup> Case T-13/99 *Pfizer Animal Health v. Council*, ECLI:EU:T:2002:209.

<sup>236</sup> Case T-13/99 *Pfizer Animal Health v. Council*, ECLI:EU:T:2002:209, para. 159.

<sup>237</sup> Section 3.2.

well as referring to independence from the regulated industry.<sup>238</sup>

Following on from the analysis above, the core principles identified as main focal points of EU administrative law that could be applied to the assessment of global standard-setting procedures are:

- participation,
- transparency, and
- independent expertise.<sup>239</sup>

However, these core principles of European administrative law and good governance are also only filled with substantive rules on how they should be applied to a certain degree, either through legislation or through case law. Establishing the full set of procedural rules of European administrative law lending itself to the legitimacy assessment of global standards requires the assessment of policy sector-specific rules, applying to administrative bodies like the Commission and active agencies is a specific regulatory field such as pharmaceuticals regulation.<sup>240</sup>

One needs to evaluate the policies and practices of the EU administrative actors in order to uncover how the treaty principles are applied in specific policy areas. It has been pointed out that some of the agencies founding regulations provide procedural rules such as consultation requirements. Internal rules and the policies that agencies set themselves need to be taken into account for a comprehensive picture. For example, the Treaty provision on access to documents provides that '[e]ach institution, body, office or agency shall ensure that its proceedings are transparent and shall elaborate in its own Rules of Procedure specific provisions regarding access to its documents'.<sup>241</sup> Generally, the transparency policies of regulatory agencies are diverse due to their different regulatory fields and task. However, some agencies provide access to the opinions of their scientific committees or declarations of interest of their staff, and agencies engage in active communication through websites.<sup>242</sup> In a study regarding the proceduralisation of rule-making powers, Chiti shows that where agencies are mandated to adopt binding implementing rules, there is a tendency to lay down certain basic procedural rules that are applied either in the founding regulation or in rules of procedure.<sup>243</sup> In soft law activities, the degree of proceduralisation is lower. However, where procedures applicable to soft law are established, they seem to mirror the rules applicable to binding measures, with a strong basis in the principles of participation and transparency.<sup>244</sup>

Thus, in order to fully assess the legitimacy of global standard-setting activities against EU procedural standards, it is necessary to not only use the Treaty provisions as a

<sup>238</sup> E. Vos, 'European Agencies and the Composite EU Executive', in M. Everson, C. Monda & E. Vos (Eds.), *European Agencies In Between Institutions and Member States* (Alphen aan den Rijn: Kluwer Law International, 2014), pp. 11-47, p. 37.

<sup>239</sup> For a similar approach see: Röhl (2007), p. 339; Ruffert (2012), p. 1214; M. Eifert, '§19 Regulierungsstrategien', in W. Hoffmann-Riem, E. Schmidt-Aßmann & A. Voßkuhle (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 1319-1394, p. 1353.

<sup>240</sup> On the importance of policy specific rules in EU administrative law see: Hofmann, Schneider & Ziller (2014), p. 46f.; Hofmann (2009), p. 50; Research Network on European Administrative Law (ReNEUAL), 'Introduction to the ReNEUAL Model Rules/ Book I – General Provisions', (2014), p. 8.

<sup>241</sup> Art. 15(3) TFEU.

<sup>242</sup> See: Hofmann, Rowe & Türk (2011), p. 300ff.

<sup>243</sup> E. Chiti, 'European Agencies' Rulemaking: Powers, Procedures and Assessment', 19(1) *European Law Journal* (2013), pp. 93-110, p. 101.

<sup>244</sup> Chiti (2013), p. 101f.

benchmark, but to look into the detailed procedural rules developed by the EU agencies active in this field of regulation. For this research, that means that an analysis of the implementation of global standards in the EU and the assessment of their legitimacy from the perspective of EU administrative law requires both a careful analysis of the standard-setting procedure on the global level, and a detailed evaluation of this procedure against the administrative procedural standards applicable in the respective policy field. As the focus of this research is the regulation of pharmaceuticals, this field and the applicable procedural rules will be analysed in detail in the following chapters.

## 6. CONCLUSION

Legitimacy was introduced as a multi-faceted concept that, beyond the notion of democracy, can contain a variety of procedural and substantive factors which have to be applied to the body in question according to its context, taking into account how the body exercises authority, and on which level of the complex interactions of governance it is established.

Accordingly, in this chapter it was established that governance through global standard-setting raises questions of legitimacy, which cannot be answered in terms of traditional national or international law. These legitimacy questions, however, are important to consider since these standards – irrespective of their voluntary nature – are adhered to and implemented in national or regional regulatory frameworks, and ultimately have an effect on the rights and duties of individuals. Moreover, global standards should not be dismissed too quickly from closer assessment due to their presumably ‘merely’ technical or scientific nature, as they often also contain political choices, especially in the risk regulation field.

It has been shown that the input legitimacy on the global level is often flawed by procedures that are neither transparent nor open to the participation of all concerned actors, thus failing to compensate for the lack of democratic legitimacy. These standards are then argued to be legitimised through their efficiency and effectiveness in addressing risks globally. However, this logic of legitimisation via output legitimacy meets its limits where, as in the case of risk regulation, there is not necessarily a ‘good’ or ‘most effective’ solution to a regulatory problem. Instead a verdict on the efficiency and effectiveness of a certain standard will very much depend on methodological choices or the perception of risks in certain societies, which means that output legitimacy cannot provide a sufficient basis of legitimisation for risk regulation standards.

Therefore, the research advocates framing the legitimacy questions addressed to global standard-setting in terms of legal-rational legitimacy derived from the conformity with administrative law. Whereas currently no established international or global administrative law exists, its evolution has become the object of recent scholarly interest. The global administrative law scholarship has made a very valuable contribution in identifying core principles as they are forming. However, global administrative law currently cannot provide a sufficient basis for a detailed substantive assessment of global standard-setting activities. The international administrative law scholarship takes a slightly different approach in placing the assessment of the international administrative law ‘in the making’ in the context of national administrative law, in order to establish procedural standards.

In the context of these debates, the approach advocated by this research is to take a European perspective, applying EU administrative law to the standard-setting processes on the global level. Although seemingly counterintuitive at first, this approach is, first of all, imperative from a EU law perspective given the effects that these standards have in the European risk regulation framework. Second of all, it is argued that EU administrative law can serve as a source of inspiration for the development of administrative rules on the global

level. Thus, as well as increasing the legitimacy of EU implementation of global standards, an EU administrative law perspective can contribute to establishing a framework to assess and improve the legitimacy of the global standard-setting process itself.

With regard to the application of EU administrative law to the global standard-setting processes, three relevant core principles were identified: transparency, participation, and independent expertise. However, it was also pointed out that although EU administrative law – like the evolving global administrative law – is largely based on general principles, these principles have been proceduralised differently in the respective policy areas, as well as through their formalisation in the Treaties and case law. Thus, where the legitimacy of global standards is assessed against EU administrative law benchmarks, an in-depth study of the policy area concerned is required. This realisation is put into practice in the following chapters of this research, which are devoted to the study of global pharmaceutical standards and their implementation in the EU, and carry out a legitimacy analysis for this specific case.



## Chapter 3: The European Union's Pharmaceutical Regulation

### 1. INTRODUCTION

The assessment of the influence of global standards on the European regulation of pharmaceuticals presupposes an in-depth understanding of the regulatory framework governing pharmaceuticals in the internal market. Therefore, this chapter will examine the past and present of pharmaceutical regulation in the European Union.<sup>1</sup> In the EU, the pharmaceutical sector is a major contributor to the economy, as the Commission's last sector enquiry impressively shows. The last sector enquiry report, adopted in 2009, provides for 430 euro spending on pharmaceuticals for each European in 2007 with an increasing tendency to do so.<sup>2</sup> Moreover, pharmaceuticals at that time accounted for 2% of the European gross domestic product.<sup>3</sup> The European Federation of Pharmaceutical Industries and Associations (EFPIA) provided more recent figures, showing that in 2015 the pharmaceutical industry employed 725,000 people and had a market value at ex-factory prices of 192,000 million euros.<sup>4</sup> However, the industrial interest in the EU is only one aspect that should be considered in the pharmaceuticals regulatory policy, as the EU is also committed to a 'high level of human health protection (...) in the definition and implementation of all Union policies and activities'.<sup>5</sup>

In the context of risk regulation, pharmaceuticals are a peculiar type of product. Although they cure or treat illness for the benefit of public health, their potent effect on the body usually comes with side effects and potential hazards.<sup>6</sup> Pharmaceuticals thus have to obtain a marketing authorisation based on a positive benefit/risk assessment in order to be admitted to the internal market; this is central to the regulation of medicinal products in the Union.<sup>7</sup> In the context of EU legislation pharmaceuticals are referred to as medicinal products,<sup>8</sup> which are defined in the EU as:

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<sup>1</sup> As well as the Union's Member States, Norway, Iceland and Liechtenstein, which constitute the European Economic Area (EEA), have accepted the European pharmaceutical regulation. Wherever a binding Union act such as a Commission decision regarding a marketing authorisation is adopted, the three countries will take a corresponding decision allowing for the marketing of the product. EEA Joint Committee, Decision of the EEA Joint Committee N74/1999 of 28 May 1999 amending Protocol 37 and Annex II (technical regulations, standards, testing and certification) to the EEA Agreement, OJ L 284, 9 November 2000, pp. 65-70.

<sup>2</sup> European Commission, DG Competition, Pharmaceutical Sector Inquiry –Final Report, Adopted 9 July 2009, p. 10, available via: [http://ec.europa.eu/competition/-sectors/pharmaceuticals/inquiry/staff\\_working\\_paper\\_part1.pdf](http://ec.europa.eu/competition/-sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf), last accessed: 3 April 2017.

<sup>3</sup> European Commission, DG Competition, Pharmaceutical Sector Inquiry – Final Report, Adopted 9 July 2009, p. 10.

<sup>4</sup> EFPIA, 'The Pharmaceutical Industry in Figures – Key Data 2016', p. 3, available via: <http://www.efpia.eu/uploads/Modules/Documents/the-pharmaceutical-industry-in-figures-2016.pdf>, accessed: 3 April 2017.

<sup>5</sup> Art. 168(1) TFEU.

<sup>6</sup> E. Vos, *Institutional Frameworks of Community Health and Safety Regulation – Committees, Agencies and Private Bodies* (Oxford: Hart Publishing, 1999), p. 204.

<sup>7</sup> Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use OJ L 311, 28 November 2001, pp. 67-128, Art. 6; Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and

(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.<sup>9</sup>

Thus the presentation and the function of the product is essential in defining them as medicinal products. A multitude of cases in front of the Court of Justice further clarified the definition of medicinal products<sup>10</sup> and the demarcation with other separately regulated products such as foodstuffs, cosmetics and medical devices.<sup>11</sup> Overall, the EU can now look back on over 50 years of regulation in the field of pharmaceuticals.<sup>12</sup> It has seen progressive harmonisation – the regulatory framework in this field is ever-growing. On top of legislative measures, soft law in the form of Commission and EMA guidelines ensures the application of the same requirements for quality, safety and efficacy throughout the EU, as this chapter will demonstrate.

This chapter will first examine the history of the harmonisation of pharmaceutical regulation in the EU, focussing on the increasing regulatory harmonisation (Section 2). In Section 3, the current regulation of pharmaceuticals in the EU (Section 3.1) and the applicable institutional framework (Section 3.2) is closely analysed. Special attention is devoted to the marketing authorisation procedures as the core of the EU's pharmaceutical regulation (Section 3.3). Besides the legally binding measures, non-binding administrative measures in the form of guidelines adopted by the Commission and European Medicines Agency form an important cornerstone of pharmaceutical regulation. Section 4 is devoted to the assessment of these guidelines, providing a detailed explanation of their role in the governance of pharmaceuticals, and critically analysing their legal nature in the context of the 'soft law' concept.

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establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 136, 30 April 2004, pp. 1-33, Art. 3.

<sup>8</sup> In the course of this research the terms pharmaceuticals, medicines and medicinal products are used interchangeably to enhance readability.

<sup>9</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 1(2).

<sup>10</sup> See e.g.: Case C-35/85 *Procureure de la Republique v. Gerard Tissier*, ECLI:EU:C:1986:143; C-319/05 *Commission v. Germany*, ECLI:EU:C:2007:678.

<sup>11</sup> See e.g.: Case C-227/82 *Criminal proceeding against Leendert van Bennekom*, ECLI:EU:C:1983:354; Case C-369/88 *Criminal proceedings against Jean-Marie Delattre*, ECLI:EU:C:1991:137; Case C-140/07 *Hecht-Pharma GmbH v. Staatliches Gewerbeaufsichtsamt Lüneburg*, ECLI:EU:C:2009:5. For more detail see: P. Feldschreiber (Ed.), *The Law and Regulation of Medicines* (Oxford: Oxford University Press, 2008), p. 31. Arguably, the ambiguous demarcation between medicinal products, foodstuffs and chemicals has led to regulatory competition between the respective responsible agencies on a European level. See: K. Purnhagen, 'Competition of Agencies in European Pharmaceutical Law – Does It Exist, Is it Desirable and How to Handle it?', 1(3) *European Journal of Risk Regulation* (2010), pp. 227-238.

<sup>12</sup> The first legislative measure adopted was Council Directive 65/65/EEC of 26 January 1965, on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ 22, 9 February 1965, pp. 369-373.

## 2. THE HISTORY OF EUROPEAN PHARMACEUTICAL REGULATION – A ROCKY ROAD TO HARMONISATION

Medicinal products have been manufactured and consumed since the early history of humanity. Pharmacopoeias describing the formulation and preparation of medical products can be traced back to Ancient Egypt.<sup>13</sup> In the 19th century, states began to regulate the quality and purity of medicinal products e.g. the Sale of Food and Drugs Act 1875<sup>14</sup> in the UK or the 1906 US Federal Food and Drug Act.<sup>15</sup> However, modern pharmaceutical regulation – placing an emphasis not only on the quality of the medicinal product, but also on safety and efficacy – is a relatively young phenomenon. Until the beginning of the 1960s most countries (with the exception of the northern European states and the US) did not subject the safety and efficacy of pharmaceuticals to governmental control.<sup>16</sup>

This changed with the 1961 Thalidomide tragedy when a drug prescribed against morning sickness for pregnant women led to serious malformations in the extremities their new-borns.<sup>17</sup> Recognising the flaws in the existing scheme, European countries established regulatory bodies as well systems of pre-marketing approval of medicines in order to safeguard not only their quality, but also their safety and efficacy.<sup>18</sup> Today pharmaceuticals, which used to be only marginally subjected to regulation, are one of the most vigilantly regulated category of goods.<sup>19</sup>

After the Thalidomide disaster the EU actively aimed for the regulation of pharmaceuticals and their related risks to establish an internal market for medicinal products. However, the regulation of such a politically sensitive area as pharmaceuticals, having an impact on health as well as industrial policies, is an important trait of national sovereignty. Medicinal products soon proved to be a difficult case for the establishment of the internal market, with the free movement of goods not being easily introduced for a product as

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<sup>13</sup> See: M. Parkins, 'Pharmacological Practices of Ancient Egypt', in W. Whitelaw (Ed.), *The Proceedings of the 10th Annual History of Medicine Days, Calgary March 23rd and 24th 2001*, pp. 5-11, available via: <http://www.ucalgary.ca/uofc/Others/HOM/Dayspapers2001.pdf>, last accessed: 3 April 2017.

<sup>14</sup> UK, Sale of Food and Drugs Act 1874.

<sup>15</sup> US, Federal Food and Drugs Act 1906.

<sup>16</sup> Permanand (2006), p. 1; J. Abraham & G. Lewis, *Regulating Medicines in Europe: Competition, Expertise and Public Health* (London: Routledge, 2000), pp. 35-79. For an account of development of pharmaceutical regulation see e.g.: J. Lisman & J. Lekkerkerker, 'Four Decades of European Medicines Regulation: What Have They Brought Us?', 17(1&2) *International Journal of Risk & Safety in Medicine* (2005), pp. 73-79; Vos (1999), p. 204ff.

<sup>17</sup> For further information on the Thalidomide crisis and its effects on pharmaceutical regulation see: S. Krapohl, 'Thalidomide, BSE and the Single Market: An Historical-Institutionalist Approach to Regulatory Regimes in the EU', 46(1) *European Journal of Political Research* (2007), pp. 25-46; Feldschreiber (2008), p. 6; Boudier (2014), pp. 91-112. Interestingly, although Thalidomide was developed by a German company, Germany was amongst the countries most heavily struck with cases of malformations. It only introduced a prescription requirement for new drugs, while it only regulated the authorisation of medicines in 1971. The regulation adopted in Europe in the aftermath of Thalidomide seemed to be less strict than the laws the US enacted in the aftermath, although damages in the US were far lower as the drug was not authorized there. For a discussion of this see: D. Vogel, *The Politics of Precaution – Regulating Health, Safety and Environmental Risks in Europe and the United States* (Princeton/Oxford: Princeton University Press, 2012), p. 189ff.

<sup>18</sup> Lisman & Lekkerkerker (2005), p. 73.

<sup>19</sup> Lisman & Lekkerkerker (2005), p. 78.

thoroughly regulated on the national level,<sup>20</sup> and where, additionally, policy approaches and national interests were divergent.

The establishment of a European pharmaceutical policy was hampered by a disagreement in the Member States, as to whether such regulation should be subject to a decentralised approach through mutual recognition of national marketing authorisations, or a centralised procedure at the EU level.<sup>21</sup> In 1963, the Commission gathered representatives of various interested parties, including industry associations as well as organisations representing doctors, pharmacists, patients and trade unions, to initiate a harmonisation process.<sup>22</sup> However, at that time it appeared impossible to reach an agreement on harmonisation measures,<sup>23</sup> serving as the perfect illustration of the conflict of economic interests, and the protection of public health when it comes to regulating pharmaceuticals.

### 2.1 1965-1975: First careful steps towards a European pharmaceuticals regulation framework

The EU overcame this failed attempt under the growing realisation of the barriers to trade produced by the divergent national regulations and established a common standard for market access of medicinal products in the EU. Using Article 100 of the Treaty Establishing the European Economic Community (EEC Treaty) on the approximation of laws as a legal basis, Council Directive 65/65 aimed at counterbalancing the free movement of goods with health protection. Its preamble states ‘the primary purpose of any rules concerning the production and distribution of proprietary medicinal products must be to safeguard public health’, which must be achieved ‘by means which will not hinder the development of pharmaceutical industry’ ultimately leading to ‘the establishment and functioning of the common market’ through ‘approximation of the relevant provisions’.<sup>24</sup>

The Council Directive introduced a pre-marketing authorisation requirement for pharmaceuticals. However, it only covered proprietary medicinal products, that is, pharmaceuticals sold under specific trade names and packaging, the formulation of which is owned by a company or individual, and not generics, which are pharmaceuticals developed to be similar to an existing product. The authorisation was to be based on the assessment of the criteria of quality, safety and efficacy. Furthermore, the Council Directive provided a list of required documentation for an application. This harmonisation was meant to pave the way for future mutual recognition of marketing authorisations. However, the implementation of these general requirements left considerable discretion to the Member

<sup>20</sup> L. Hancher, *Regulating for Competition – Government, Law and the Pharmaceutical Industry in the United Kingdom and France* (Alblasserdam: Haveka, 1989), p. 103ff.

<sup>21</sup> Hancher (1989), p. 104; Vos (1999), pp. 206-207.

<sup>22</sup> L. Orzack, K. Kaitin & L. Lasagna, ‘Pharmaceutical Regulation in the European Community: Barriers to Single Market Integration’, 17(4) *Journal of Health Politics, Policy and Law* (1992), pp. 847-868, p. 853.

<sup>23</sup> *Ibidem*. The initiative failed due to industry opposition to include a requirement of proof of ‘therapeutic potency’, while this was deemed a *conditio sine qua non* by the other represented interests. According to Hancher, the question of including efficacy as a testing requirement also led to problems in the adoption of Directive 65/65/EEC, where (West) Germany, which had a strong pharmaceutical industry, first opposed introducing efficacy as a requirement. The compromise was to limit the proof of efficacy to the proof of pharmacodynamic results, so only biochemical or physiological effects had to be proven, and did not have to be positive, f.e. curing diseases. See: Hancher (1989), p. 105.

<sup>24</sup> Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ 22, 9 February 1965, pp. 369-373.

States.<sup>25</sup>

Still, Council Directive 65/65/EC marks an important step in European integration since its commitment to the safeguarding of public health deviated from the economic focus of the Treaty of Rome, in force at the time, that did not provide an explicit public health protection mandate.<sup>26</sup> The Commission aimed at following up the harmonisation with further Directives on the experts that should assess marketing authorisations, an automatic mutual recognition, and the harmonisation of the laws of advertising, all of which were never adopted.<sup>27</sup> It took the EU another 10 years to pass the next legislation in the pharmaceutical area with the adoption of Council Directives 75/318/EEC<sup>28</sup> and 74/319/EEC.<sup>29</sup>

## 2.2 1975-1985: Further integration and hampered mutual recognition

Council Directive 75/318/EEC provided more detail on the documentation required for applications to national authorities under Directive 65/65/EEC. This Council Directive was of importance due to its Annex, which contained detailed information on required trials to prove the safety as well as efficacy of a medicine, and the data that needs to be provided by the applicant in a marketing authorisation procedure. This detailed guidance in the Annex contributed to further harmonisation of the data that is the basis of the quality, safety and efficacy assessment in a marketing authorisation. This harmonisation of technical and scientific requirements was an important step towards the approximation of the regulatory systems of the Member States.<sup>30</sup>

The adoption of Council Directive 75/319/EEC also represented a further step towards the integration of the European pharmaceuticals market: it introduced the community procedure. Through this procedure the free movement of pharmaceuticals within the EU was supposed to be achieved by mutual recognition. However, the community procedure did not entail the automatic mutual recognition of a product authorised in one Member State in all the other Member States. Instead it provided the opportunity for a company that had obtained the marketing authorisation in one Member State, to apply for approval in at least five other Member States, on the basis of the evaluation of the first state.<sup>31</sup> These five receiving Member States could subsequently issue a marketing authorisation, taking the authorisation issued by the reference Member State into account. Importantly, this Directive established the Committee for Proprietary Medicinal Products (CPMP), which was composed of national representatives and set up in order to advise national authorities on the authorisation of medicinal products.<sup>32</sup> In case of objection, on the side of a Member State to authorise a product under the community procedure, the

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<sup>25</sup> J. Feick, 'Learning and Interest Accommodation in Policy and Institutional Change: EC Risk Regulation in the Pharmaceutical Sector', ESCR Centre for Analysis of Risk and Regulation (CARR) Discussion Paper 25, (January 2005), p. 7.

<sup>26</sup> National Institute for Public Health and the Environment, 'Minds Open – Sustainability of the European Regulatory System for Medicinal Products', RVIM-Report 2014-0033, p. 15.

<sup>27</sup> Hancher (1989), p. 106.

<sup>28</sup> Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products OJ L 147, 9 June 1975, pp. 1-12.

<sup>29</sup> Second Council Directive 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products OJ L 147, 9 June 1975, pp. 13-22.

<sup>30</sup> Lisman & Lekkerkerker (2005), p. 75.

<sup>31</sup> Hancher (1989), p. 107.

<sup>32</sup> Second Council Directive 75/319/EEC, OJ L 147, 9 June 1975, pp. 13-22, Art. 8.

CPMP could pass a non-binding, advisory opinion on the issue.<sup>33</sup>

However, the procedure was neither favoured by industry nor by the national authorities. In the eight years it operated, only 41 applications were filed<sup>34</sup> and they were hampered by the fact that the states were unwilling to accept each other's assessment, so that there was literally no procedure without an objection from the receiving states.<sup>35</sup> Even the reformation of the procedure through Council Directive 83/570/EEC,<sup>36</sup> transforming it into the so-called multi-state procedure with a reduced number of required receiving states to two, did not lead to greater success in terms of Member States accepting each other's assessment. The Commission concluded that the practice of the multi-state procedure 'is not consistent with the spirit of the directive which introduced it',<sup>37</sup> which clearly indicates the struggle that regulatory harmonisation in the field of pharmaceuticals was facing.

### 2.3 1985-1995: Goal of a single market by 1992

The harmonisation of the pharmaceuticals regulation gained new impetus due to the Single European Act and the envisaged goal of a single market by 1992.<sup>38</sup> In the White Paper on the Completion of the Single Market from 1985, the Commission had already committed to a unified market for medicines by 1992.<sup>39</sup> At this point in time, the harmonisation process was still severely hampered by the persisting difference in the evolution of the marketing authorisation applications and delay in the national procedures.<sup>40</sup>

The introduction of the concentration procedure with Council Directive 87/22/EEC<sup>41</sup> was meant to facilitate discussion of divergent views in the Member States, while leaving the final decision on authorisation to the Member States individually.<sup>42</sup> The procedure applied compulsorily for biotechnological medicines and optionally for other innovative or highly technological medicines. It required the companies' applications to be filed with one national authority as well as with the CPMP. The evaluation was subsequently discussed within the framework of the CPMP. The CPMP's final opinion was, however, not binding upon the

<sup>33</sup> Second Council Directive 75/319/EEC, OJ L 147, 9 June 1975, pp. 13-22, Art. 11.

<sup>34</sup> European Commission, Report from the Commission to the Council on the Activities of the Committee for Proprietary Medicinal Products, COM(91)39 final, Brussels, 15 February 1991, p. 14.

<sup>35</sup> European Commission, Report from the Commission to the Council on the Activities of the Committee for Proprietary Medicinal Products, COM(91)39 final, Brussels, 15 February 1991, p. 16.; Vos (1999), p. 209.

<sup>36</sup> Council Directive 83/570/EEC of 26 October 1983 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ L 332, 28 November 1983, pp. 1-10.

<sup>37</sup> European Commission, Report from the Commission to the Council on the Activities of the Committee for Proprietary Medicinal Products, COM(91)39 final, Brussels, 15 February 1991, p. 16.

<sup>38</sup> Single European Act, OJ L 169, 29 June 1987, pp. 1-29.

<sup>39</sup> European Commission, White Paper from the Commission to the European Council – Completing the Internal Market, COM(85) 310 final, Brussels, 14 June 1985.

<sup>40</sup> P. Cecchini, *The European challenge 1992 – Benefits of a Single Market* (Aldershot: Wildwood House, 1988), p. 68.

<sup>41</sup> Council Directive 87/22/EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology, OJ L 15, 17 January 1987, pp. 38-41.

<sup>42</sup> L. Hancher, 'Creating the Internal Market for Pharmaceutical Medicines – An Echternach Jumping Procession?', 28(4) *Common Market Law Review* (1991), pp. 821-853, p. 824.

Member States.<sup>43</sup> The Member States still adopted their own marketing authorisation; yet, diverging from the CPMP opinion was rather difficult.<sup>44</sup> This procedure was more successful than previous attempts,<sup>45</sup> which might be due to the fact that the biotechnological products were subjected to a procedure that was different to 'normal' medicinal products and had a less extensive regulatory legacy.<sup>46</sup>

In the following years the scope of European pharmaceutical legislation was further extended to generic medicinal products,<sup>47</sup> and other specific categories of pharmaceuticals.<sup>48</sup> Furthermore, the 'Rational Use' package broadened the existing focus of assessment of pharmaceutical risks to include risk management measures too,<sup>49</sup> for example, with regard to labelling<sup>50</sup> or advertising.<sup>51</sup> However, the single market for medicinal products had still not been achieved. An automatic mutual recognition of marketing authorisations remained a distant prospect.

Therefore, the Commission entered into discussions with stakeholders like the national agencies, the industry and – to a lesser extent – consumer associations, in order to reform the European marketing authorisation system.<sup>52</sup>

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<sup>43</sup> Council Directive 87/22/EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology, OJ L 15, 17 January 1987, pp. 38-41, Art. 4.

<sup>44</sup> Lisman & Lekkerkerker (2005), p. 76.

<sup>45</sup> Hancher (1991), p. 824.

<sup>46</sup> Vos (1999), p. 209; National Institute for Public Health and the Environment, 'Minds Open – Sustainability of the European Regulatory System for Medicinal Products', RVIM-Report 2014-0033, p. 17.

<sup>47</sup> Council Directive 89/341/EEC of 3 May 1989 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ L 142, 25 May 1989, pp. 11-13.

<sup>48</sup> The extension of scope covered radiopharmaceuticals (Council Directive 89/343/EEC of 3 May 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for radiopharmaceuticals, OJ L 142, 25 May 1989, pp. 16-18), immunological medicinal products (Council Directive 89/342/EEC of 3 May 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for immunological medicinal products consisting of vaccines, toxins or serums and allergens, OJ L 142, 25 May 1989, pp. 14-15), blood products (Council Directive 89/381/EEC of 14 June 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products and laying down special provisions for medicinal products derived from human blood or human plasma, OJ L 181, 28 June 1989, pp. 44-46) and homeopathics (Council Directive 92/73/EEC of 22 September 1992 widening the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products and laying down additional provisions on homeopathic medicinal products, OJ L 297, 13 October 1992, pp. 8-11).

<sup>49</sup> Lisman & Lekkerkerker (2005), p. 76; National Institute for Public Health and the Environment, 'Minds Open – Sustainability of the European regulatory system for medicinal products', RVIM-Report 2014-0033, p. 18.

<sup>50</sup> Council Directive 92/27/EEC of 31 March 1992 on the labelling of medicinal products for human use and on package leaflets, OJ L 113, 30 April 1992, pp. 8-12.

<sup>51</sup> Council Directive 92/28/EEC of 31 March 1992 on the advertising of medicinal products for human use OJ L 113, 30 April 1992, pp. 13-18.

<sup>52</sup> Feick (2005), p. 12.

## 2.4 1993-present: *The introduction of a truly European authorisation procedure and the birth of EMA*

This reform process led to the adoption of new pieces of legislation in 1993, which by January 1995 established the system of two European procedures for pharmaceutical marketing authorisations as it is still operative today. Since the marketing authorisation procedures currently in force will be discussed in detail in Section 3, the developments from 1993 onwards are only mentioned briefly. In essence, apart from the cases where a product is supposed to be marketed in only one Member State, the following two options for a marketing authorisation have replaced the previous procedures in 1995: the mutual recognition procedure and the centralised procedure.

Where a product is marketed in more than one Member State it can be authorised via the mutual recognition procedure introduced by Council Directive 93/39/EC.<sup>53</sup> Here it will suffice to mention that, learning from the history of procedures introduced before, this procedure allows for binding arbitration on the European level if the Member States are unable to agree on the granting or refusal of a marketing authorisation. Most importantly, however, the reform introduced a truly European, centralised procedure, which allows for actual binding marketing authorisations on an EU level.<sup>54</sup> The step from negative to positive integration through introducing a marketing authorisation on an EU level cannot be underestimated. Moreover, with the European Medicines Evaluation Agency (now European Medicines Agency, EMA), a new European Agency was set up as a focal point in the marketing authorisation procedure through Regulation 2309/39/EEC, which integrated the CPMP as its scientific body.

After the evaluation of the new procedures in October 2000<sup>55</sup> and a review of the existing legislative framework, the Directives governing medicinal products were consolidated, which led to the adoption of Directive 2001/83/EC.<sup>56</sup> Later the legislation of the centralised procedure was also updated through the implementation of Regulation (EC) 726/2004.<sup>57</sup> Another more recent milestone in the framework was the proposal of the so-called ‘pharmaceuticals package’ with proposed legislation on access to reliable information on medicines,<sup>58</sup> pharmacovigilance (safety monitoring),<sup>59</sup> and counterfeit medicines.<sup>60</sup>

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<sup>53</sup> Council Directive 93/39/EEC of 14 June 1993 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC in respect of medicinal products, OJ L 214, 24 August 1993, pp. 22-30.

<sup>54</sup> Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products, OJ L 214, 24 August 1993, pp. 1-21).

<sup>55</sup> European Commission, Report from the Commission on the experience acquired as a result of the operation of the procedures for granting marketing authorisations for medicinal products laid down in Regulation (EEC) N° 2309/93, in chapter III of directive 75/319/EEC and chapter IV of directive 81/851/EEC, COM(2001) 606 final, Brussels, 23 October 2001.

<sup>56</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128.

<sup>57</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33.

<sup>58</sup> The proposals for the amendment of the Directive 2001/83/EC and Regulation (EC) 726/2004 as regards information to the general public on medicinal products were withdrawn in May 2014 (OJ CL 158, 21 May 2014, p. 3).

<sup>59</sup> Adopted as: Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 348, 31 December 2010, pp. 74-99; Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human

To conclude, the history of European integration of pharmaceutical regulation until today has been a rocky road of continuous reformation and step by step centralisation of decision-making power. It is proof of the reluctance of states to trust the regulatory systems of other states in an area as politically sensitive as pharmaceuticals, which touches upon the public health policy and industrial policy.<sup>61</sup> However, it is also a story of slowly increasing the mutual trust through regulatory cooperation, both in the framework of the decentralised and centralised route of marketing authorisation.<sup>62</sup> The next section will examine the framework of pharmaceutical regulation currently in force in the EU. Special attention will be paid to the marketing authorisation procedures currently in force, since they form the core of the European regulatory framework.

### 3. REGULATION OF PHARMACEUTICALS IN THE EU AND MARKETING AUTHORISATION PROCEDURES

Under the current Lisbon Treaty framework, the competence for the EU's actions in the field of pharmaceuticals is based on the shared competences of regulating the internal market (Article 4(2)(a) TFEU) and Article 4(2)(k) TFEU, which covers 'common safety concerns in public health matters, for the aspects defined in this Treaty'. It should be noted that the protection and improvement of human health in general only provides the EU with a supportive capacity according to Article 6(a) TFEU). The legal basis for the adoption of EU legislation in the field of pharmaceuticals is to be found in the approximation of laws provision: Article 114 TFEU in conjunction with Article 168(4) TFEU. This allows for EU legislative action in order to contribute to the achievement of public health objectives through '(m)asures setting high standards of quality and safety for medicinal products and devices for medical use'.

#### 3.1 *Current legislative framework of European pharmaceutical regulation*

More than 50 years after the adoption of the first legislative measure of European pharmaceuticals policy – Council Directive 65/65/EC – the EU now operates an extensive system of pharmaceutical regulation. The legally binding measures are assembled in Eudrax Volume 1,<sup>63</sup> which contains the collection of pharmaceutical legislation for medicinal products for human use, and legally binding measures adopted by the Commission.

The two most important instruments of the EU's pharmaceutical framework are Directive 2001/83/EC, on the Community code relating to medicinal products,<sup>64</sup> and Regulation (EC) 726/2004/EC, governing the centralised marketing authorisation procedure on the European level.<sup>65</sup> These two legislative measures form the core of European

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use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 348, 31 December 2010, pp. 1-16.

<sup>60</sup> Adopted as: Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products, OJ L 174, 1 July 2011, pp. 74-87.

<sup>61</sup> Hancher (1989), p. 131; Feick (2005), p. 16ff.

<sup>62</sup> Feick (2005), p. 23; Vos (1999), p. 249.

<sup>63</sup> [http://ec.europa.eu/health/documents/eudrax/vol-1/index\\_en.htm](http://ec.europa.eu/health/documents/eudrax/vol-1/index_en.htm), last accessed: 3 April 2017.

<sup>64</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128.

<sup>65</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33.

pharmaceuticals regulation and provide for marketing authorisation procedures. This main legislative framework has been supplemented through various other legislative measures, the most important being Regulation (EC) 141/2000 on orphan medicinal products,<sup>66</sup> Regulation 536/2014 on clinical trials,<sup>67</sup> and specific legislation for medicines for children,<sup>68</sup> herbal medicinal products,<sup>69</sup> and advanced therapy medicinal products.<sup>70</sup> With the regulation of authorisation procedures, the European regulatory framework for pharmaceuticals has developed into an extensive and complex set of rules, dealing with areas of labelling and packaging,<sup>71</sup> as well as wholesale<sup>72</sup> and advertising.<sup>73</sup>

In addition, extensive rules on the monitoring of the safety of medicinal products, namely pharmacovigilance, are put into place.<sup>74</sup> The Commission has adopted an array of non-legislative measures in the form of Commission Regulations and Directives, and (since the Lisbon Treaty) Commission Delegated or Implementing Regulations and Decisions. These are legally binding but do not follow the legislative procedure as decision-making has been delegated to the Commission.<sup>75</sup> Currently, the legally binding framework for medicinal products for human use consists of 13 legislative acts and 17 non-legislative acts.<sup>76</sup> Apart

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<sup>66</sup> Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, OJ L 18, 22 January 2000, pp. 1-5.

<sup>67</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, OJ L 158, 27 May 2014, pp. 1-76.

<sup>68</sup> Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ L 378, 27 December 2006, pp. 1-19.

<sup>69</sup> Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 136, 30 April 2004, pp. 85-90.

<sup>70</sup> Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ L 324, 10 December 2007, pp. 121-137.

<sup>71</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 54-69.

<sup>72</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 76-85b.

<sup>73</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 86-100.

<sup>74</sup> Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 348, 31 December 2010, pp. 74-99; Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use, and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 348, 31 December 2010, pp.1-16.

<sup>75</sup> For more details on delegated and implementing acts see: P. Craig, 'Delegated Acts, Implementing Acts and the New Comitology Regulation', 36(5) *European Law Review* (2011), pp. 671-687; H. Hofmann & A. Türk, 'Die Ausübung übertragener Normsetzungsbefugnisse durch die Europäische Kommission: Verfahrensrecht in einer neuen Dimension', 27(2) *Zeitschrift für Gesetzgebung* (2012), pp. 105-137.

<sup>76</sup> These measures are listed on the Commission's Eudralex website which compiles the Union's pharmaceutical regulatory framework. The numbers provided in the text reflect the information provided at: [http://ec.europa.eu/health/documents/eudralex/vol-1/index\\_en.htm#nla](http://ec.europa.eu/health/documents/eudralex/vol-1/index_en.htm#nla), last accessed: 3 April 2017.

from the legislative and non-legislative measures, the European pharmaceuticals framework constitutes extensive guidance through non-legally binding acts – guidelines adopted by the Commission and the European Medicines Agency. They often contain pharmaceutical standards on the European level and serve the implementation of global standards, and will be discussed in detail later in this chapter.<sup>77</sup> Thus, a mix of several legally binding and non-binding forms of regulation is applied to regulate pharmaceuticals extensively in the EU.

Overall, the focus of European pharmaceutical regulation is and will for the foreseeable future remain on internal market aspects in conjunction with the free movement of goods and the establishment of safety, quality and efficacy, focusing on harmonisation of marketing authorisation procedures and leaving for example price and reimbursement issues to the Member States.<sup>78</sup> This, in particular, is owing to the sovereignty of the Member States to determine their health policy and organise their health care system as enshrined in Article 168(7) TFEU. Thus, 50 years after the first steps into the EU regulation of pharmaceuticals was taken, the completion of the single market in pharmaceuticals has not been accomplished.<sup>79</sup>

### 3.2 *The institutional framework of the European executive in pharmaceutical regulation: the Commission and the EMA*

Since the European Commission and the European Medicines Agency are key actors in the day-to-day execution of pharmaceuticals regulation, responsible for the correct application of legislative measures, they will be briefly introduced here.

The European Commission has a significant say in the formation of the content of European pharmaceutical regulation through the right of legislative initiative contained in Article 17(2) TEU, and the possibility to shape pharmaceutical policy through various soft law means.<sup>80</sup> It also monitors the correct application of legislation (Article 17(1) TEU), especially in the Member States, and is responsible for taking binding decisions on marketing authorisations for pharmaceutical products.<sup>81</sup> The Commission is also responsible for adopting marketing authorisation decisions for centrally authorised pharmaceutical products, as will be discussed in the next section.

Within the Commission, the Directorate General for Health and Food Safety (DG

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<sup>77</sup> Section 4.

<sup>78</sup> G. Permanand & C. Altenstetter, 'The Politics of Pharmaceuticals in the European Union', in E. Mossialos, M. Mrazek & T. Walley (Eds.), *Regulating Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality* (Maidenhead: Open University Press, 2004), pp. 38-54. Even though the pricing of medicinal products remains a Member State competence, the Union adopted Council Directive 89/105/EEC of 21 December 1988, relating to the transparency of measures regulating the prices of medicinal products for human use, and their inclusion in the scope of national health insurance systems (OJ L 40, 11 February 1989, pp. 8-11) to counteract hidden quantitative restrictions through pricing systems.

<sup>79</sup> However, the Commission is striving for the completion of the internal market especially to ensure equal access to pharmaceuticals in all Member States, and for the benefit of the pharmaceutical industry in Europe. See: European Commission, Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector, COM(2008) 666 final, Brussels, 10 December 2008, p. 4.

<sup>80</sup> For a detailed account of the Commission's powers to adopt soft law see: Senden (2003), pp. 315-341.

<sup>81</sup> See: Section 4.

SANTE) is responsible for pharmaceuticals since the Barroso Commission in 2009.<sup>82</sup> Before that, the responsibility lay with the Directorate General Enterprise, a constellation that was criticised for facilitating the prioritisation of industrial concerns over public health issues.<sup>83</sup> A proposal by Commission President Juncker to transfer responsibilities back to DG Enterprise in 2014 was received with great scepticism and critique,<sup>84</sup> ultimately convincing Juncker to reconsider his proposal and leave pharmaceutical regulation with DG SANTE.<sup>85</sup>

As well as the Commission, the European Medicines Agency (EMA) is an important actor in the EU's pharmaceutical regulation. The agency was set up on 22 July 1993 as a 'culmination of thirty years of pharmaceutical legislation',<sup>86</sup> and became operational in January 1995.<sup>87</sup> It is one of the EU's 'non-majoritarian agencies'<sup>88</sup> created as 'satellite' bodies surrounding the executive, in order to infuse the decision-making process with independent scientific and technical expertise.<sup>89</sup> Amongst others, the specific tasks of the EMA comprise the 'coordination of the scientific evaluation of the quality, safety and efficacy of medicinal products which are subject to Community marketing authorisation procedures' and the coordination of pharmacovigilance measures.<sup>90</sup> It has a central role in the marketing authorisation procedure, as will be assessed below.

The agency coordinates the national agencies tasked with the authorisation of

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<sup>82</sup> European Commission, Press Release – Barroso unveils his new team, Brussels 27 November 2009, available via: [http://europa.eu/rapid/press-release\\_IP-09-1837\\_en.htm?locale=en](http://europa.eu/rapid/press-release_IP-09-1837_en.htm?locale=en), last accessed: 3 April 2017. The DG used to be called DG SANCO (for Health and Consumers), but was renamed in the Juncker Commission.

<sup>83</sup> European Public Health Alliance, MEPs support health community call for Health Commissioner to 'own' pharmaceutical policy, available via: <http://v3.epha.org/spip.php?article3542>, last accessed: 3 April 2017. See also: Permanand (2006), p. 38.

<sup>84</sup> Euractiv, 'A bad start for the new Commission', 11 September 2015, available via: <http://www.euractiv.com/sections/health-consumers/bad-start-new-commission-308376>, last accessed: 3 April 2017; Euractiv, 'Why Juncker should backtrack and keep pharma policy in the health portfolio', 18 September 2014, available via: <http://www.euractiv.com/sections/health-consumers/why-juncker-should-backtrack-and-keep-pharma-policy-health-portfolio>, last accessed: 3 April 2017; European Public Health Alliance, [Open letter] To President-elect Jean Claude Juncker on the move of medicinal products and health technologies to the portfolio of the Commissioner for internal market and industry, 16 September 2014, available via: <https://epha.org/open-letter-to-president-elect-jean-claude-juncker-on-move-of-medicinal-products-and-health-technologies-to-the-portfolio-of-the-commissioner-for-internal-market-and-industry>, last accessed: 3 April 2017.

<sup>85</sup> Euractiv, 'Juncker turn puts pharma in health Commissioner portfolio', 22 October 2014, available via: <http://www.euractiv.com/sections/health-consumers/juncker-u-turn-puts-pharma-health-commissioners-portfolio-309396>, last accessed: 3 April 2017.

<sup>86</sup> M. Groenleer, *The Autonomy of European Union Agencies – A Comparative Study of Institutional Developments* (Delft: Eburon, 2009), p. 143.

<sup>87</sup> The EMA was created through Council Regulation (EEC) No 2309/93 OJ L 214, 24 August 1993, pp. 1-21. This Council Regulation was replaced by Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, which now regulates the mandate and functioning of the EMA.

<sup>88</sup> The notion 'non-majoritarian agencies' is used to refer to the fact that although carrying out a public function, these bodies are independent from elected politicians. See: D. Curtin, 'Delegation to EU Non-Majoritarian Agencies and Emerging Practices of Public Accountability', in D. Geradin, R. Munoz & N. Petit (Eds.), *Regulation Through Agencies in the EU: A New Paradigm of European Governance* (Cheltenham: Edward Elgar, 2006), pp. 88-119, p. 92.

<sup>89</sup> Curtin (2009), p. 52.

<sup>90</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 57.

pharmaceuticals to ensure a harmonised approach. This makes the EMA the centre of a large regulatory network of national regulatory authorities.<sup>91</sup> After consultation with the Agency's Management Board, each of the Member States appoints a member and an alternate to form the scientific committees that carry out the assessments within the agency, chosen 'for their role and experience in the evaluation of medicinal products'.<sup>92</sup> The former Committee for Proprietary Medicinal Products (CPMP), introduced in Section 2, was renamed the Committee for Medicinal Products for Human Use (CHMP) in 2004, and forms the main scientific committee for evaluating medicines for humans. As well as the CHMP, the Committee for Medicinal Products for Veterinary Use (CVMP), the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC), the Committee for Advance Therapies (CAT) and the Paediatric Committee (PDCO) evaluate pharmaceuticals.<sup>93</sup>

How the Commission and the European Medicines Agency interact with each other and the national regulatory authorities in marketing authorisation procedures, forming the heart of pharmaceuticals regulation in the EU, will be subject to closer assessment in the following sub-section.

### 3.3 *Marketing authorisation procedures*

As established before, the core of EU pharmaceutical regulation is the marketing authorisation requirement. While no medicinal product may be placed on the market without obtaining prior marketing authorisation,<sup>94</sup> under the current system a pharmaceutical company can follow different routes to obtain a marketing authorisation for a medicinal product in the Union:

- centralised procedure: This procedure is mandatory for certain biotechnology-derived and high-tech products, and optional for products with a new active substance or products offering a significant therapeutic, scientific or technical innovation.<sup>95</sup> The marketing authorisation is granted on the EU level by the Commission. The scientific assessment of the application is carried out centrally at the level of the European Medicines Agency. Thus, the procedure is truly European.
- mutual recognition/decentralised procedure: These procedures are laid down in Directive 2001/83/EC, and are available in case a medicinal product is to be marketed in more than one Member State.<sup>96</sup> As will be examined in detail in

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<sup>91</sup> For further detail on the network character of the European Medicines Agency see: Dehousse (1997), pp. 246-261; A. Spina, 'The Regulation of Pharmaceuticals Beyond the State: EU and Global Administrative Systems', in E. Chiti & B. Mattarella (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer, 2011), pp. 249-268.

<sup>92</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 61(1).

<sup>93</sup> The legal basis for the establishment of these Committees is Regulation (EC) No 726/2004 OJ L 136, 30 April 2004, pp. 1-33, Art. 56. For more information on the Committees see: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/-general/general\\_content\\_000217.jsp&mid=](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/-general/general_content_000217.jsp&mid=), last accessed: 3 April 2017.

<sup>94</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 6; Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 3.

<sup>95</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 3 jo. Annex.

<sup>96</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 28-39.

Section 3.3.2, the procedures contain European elements, but the final decision is still taken at a national level.

- national: As the European marketing authorisation does not replace national ones, it is still possible for manufacturers to follow national procedures in case the product will be sold in one Member State only, and does not belong to the categories of products for which the centralised procedure is obligatory.<sup>97</sup> The national route for marketing authorisations is still frequently used and in some countries even constitutes the largest number of authorisation applications.<sup>98</sup> However, the national marketing authorisation procedures are also subject to harmonisation, for example in terms of duration and required documentation.<sup>99</sup>

Accordingly, the routes to obtaining marketing authorisation in the EU are diverse. The applicability of the procedures depends on the nature of the medicinal product in question and the targeted state market(s). This divergence in degree of integration and ‘institutional layering’<sup>100</sup> in the regulation of one single type of product is certainly remarkable in the context of the internal market. However, although the routes to obtaining a marketing authorisation are diverse, the requirements for the applicant to prove quality, safety and efficacy and the basic traits of the procedure in the respective authority are subject to European harmonisation.<sup>101</sup>

### 3.3.1 Centralised marketing authorisation procedure

One route to obtaining a marketing authorisation is the centralised procedure which is laid down in Regulation (EC) 726/2004. This procedure is carried out at the European level, leading to one authorisation which is valid in the whole of the EU. However, the centralised procedure is only obligatory for certain medicinal products that are defined in the Annex to the Regulation.<sup>102</sup> Those that are medicines for humans are: (i) biotechnologically developed pharmaceuticals; (ii) advanced therapy medicinal products as defined in Regulation 1394/2007;<sup>103</sup> (iii) products with a new active substance (not authorised before the Regulation entered into force) for the treatment of certain diseases, such as for example cancer or autoimmune diseases; as well as (iv) orphan medicinal products – pharmaceuticals targeting serious diseases that affect only up to 5 in ten thousand people.<sup>104</sup> The procedure is optional for all other products with new active substances, as well as pharmaceuticals with a significant therapeutic, scientific or technical innovation, or where the authorisation is of interest at EU level.<sup>105</sup>

<sup>97</sup> Regulation (EC) No 726/2004 OJ L 136, 30 April 2004, pp. 1-33, Art. 6 jo. 17 and 18.

<sup>98</sup> Feick (2005), p. 12.

<sup>99</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 17-27.

<sup>100</sup> Feick (2005), p. 19.

<sup>101</sup> See also: EMA, The European regulatory system for medicines and the European Medicines Agency – A consistent approach to medicines regulation across the European Union, (2014), EMA/437313/2014.

<sup>102</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 3(1).

<sup>103</sup> Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ L 324, 10.12.2007, pp. 121-137.

<sup>104</sup> Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, OJ L 18, 22.1.2000, pp. 1-5.

<sup>105</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 3(2). The reference to ‘Community interest’ in the Regulation should now be read as reference to ‘Union interest’.

In these cases the company files a marketing authorisation application, the so-called dossier, including the documentation required with the EMA.<sup>106</sup> The application is then assessed in the main scientific committee for human medicinal products, the CHMP. Following the rules of procedure of the committee, a rapporteur appointed amongst the members is assigned the responsibility for the scientific assessment of the application, and the drawing up of a report with the help of experts from a list provided by the EMA.<sup>107</sup> A co-rapporteur is nominated who will either prepare a critical assessment of the report drawn up by the rapporteur, or will write an assessment report, depending on the choice of the Committee.<sup>108</sup> Once the rapporteur has drafted the report, it is sent to the Committee, which establishes whether the application fulfils the requirements of Directive 2001/83, and may request further information from the applicant.<sup>109</sup> Subsequently, the Committee adopts a favourable or unfavourable opinion, if possible by consensus, but at least by absolute majority.<sup>110</sup> In case the opinion is unfavourable, Article 9 of Regulation (EC) 726/2004 provides that the applicant is informed before. In case of a negative opinion, the applicant can request a re-examination within 15 days upon receipt of the opinion, and substantiate this request with detailed reasoning within 60 days.<sup>111</sup> Then, the opinion is re-examined by the Committee (with a different rapporteur) within 60 days.<sup>112</sup>

Thus, after 210 days of the procedure at the latest, the agency gives a favourable or unfavourable opinion on the marketing authorisation and forwards it to the Commission.<sup>113</sup> It is important to note that the opinion is of advisory nature and the decision-making power in case of marketing authorisations lies with the Commission, and not the agency. Upon receipt of the EMA opinion, the Commission drafts a decision within 15 days.<sup>114</sup> If the draft decision departs from the EMA opinion, this has to be substantiated by the Commission.<sup>115</sup> In practice, the Commission usually follows the CHMP opinion.<sup>116</sup> A notable exception was the disagreement between the EMA and the Commission over the drug Orphacol, which

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<sup>106</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 6.

<sup>107</sup> Committee for Medicinal Products for Human Use, Rules of Procedure, EMEA/45110/2007, Art. 6.

<sup>108</sup> Committee for Medicinal Products for Human Use, Rules of Procedure, EMEA/45110/2007, Art. 6(3).

<sup>109</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 7. A detailed account of the procedure within the CHMP can be found in the Notice to Applicants. See: European Commission, Notice to Applicants, Volume 2A Procedures for marketing authorisation, Chapter 4 Centralised Procedure, Brussels, April 2006, ENTR/F2/BL D(2006), available via: [http://ec.europa.eu/health/documents/eudralex/vol-2/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm), last accessed: 3 April 2017.

<sup>110</sup> Committee for Medicinal Products for Human Use, Rules of Procedure, EMEA/45110/2007, Art. 8. Additionally, Regulation (EC) No 726/2004 provides for the possibility of granting a conditional marketing authorisation (Art. 14(7)), reviewed annually, and a marketing authorisation under exceptional circumstances (Art. 14(8)), which contains certain obligations with regard to the safety of the product.

<sup>111</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 9(2).

<sup>112</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 9 jo. 62(1).

<sup>113</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 6 jo. 9.

<sup>114</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 10.

<sup>115</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 10.

<sup>116</sup> T. Gehring & S. Krapohl, 'Supranational Regulatory Agencies between Independence and Control. The EMA and the Authorisation of Pharmaceuticals in the European Single Market', 14(2) *Journal of European Public Policy* (2007), pp. 208-226, p. 216; Feick (2005), p. 14.

although it received positive assessment from the EMA,<sup>117</sup> was initially refused marketing authorisation by the Commission.<sup>118</sup> The Court annulled the negative decision of the Commission<sup>119</sup> and Orphacol currently has the authorisation.<sup>120</sup>

The Commission's draft decision is also forwarded to Member States and the applicant.<sup>121</sup> In the following, the Member States are entitled to submit written observations to the Commission.<sup>122</sup> Where these written observations raise important scientific issues, which have been neglected in the evaluation thus far, the application will be referred back to the agency.<sup>123</sup> This is however rather unlikely since the Member State would have to show that the issue is very important and has been neglected by the applicant, the CHMP, the EMA itself and the Commission.<sup>124</sup> In the applicable examination procedure laid down in Article 5 of the Regulation (EU) 182/2011,<sup>125</sup> the Commission also forwards the draft decision to the Standing Committee on Medicinal Products for Human Use, composed of Member State representatives, which votes on the adoption of this draft decision by qualified majority.

A positive decision adopted by the Commission, in the form of a Commission implementing decision, grants a marketing authorisation valid within the whole Union for five years, meaning that the decision is binding upon the Member States.<sup>126</sup> After these five years, the marketing authorisation can be renewed when the agency carries out a renewed positive risk-benefit evaluation.<sup>127</sup> The renewed marketing authorisation then has unlimited validity, unless specified otherwise.<sup>128</sup>

This procedure is centralised at the EU level; the decision-making power lies with the European Commission, and the main scientific foundation for the decision is laid at the

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<sup>117</sup> A positive opinion was adopted by the CHMP on 16 December 2010. After a request for clarification by the Commission, the CHMP adopted a revised opinion on 14 April 2011, which was a positive opinion for granting marketing authorisation under exceptional circumstances. See: EMA, Assessment Report Orphacol, EMA/596651/2013, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Public\\_assessment\\_report/human/001250/WC500131542.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/001250/WC500131542.pdf), last accessed: 3 April 2017. The authorisation under exceptional circumstances entails that the product is subject to yearly review.

See: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001250/human\\_med\\_001419.jsp&mid=WC0b01ac058001d124](http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001250/human_med_001419.jsp&mid=WC0b01ac058001d124), last accessed: 3 April 2017.

<sup>118</sup> Commission Implementing Decision C(2012) 3306 final of 25 May 2012 refusing a marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council for "Orphacol – Cholic acid", an orphan medicinal product for human use.

<sup>119</sup> Case T-301/12 *Laboratoires CTRS v. European Commission*, ECLI:EU:C:2014:214.

<sup>120</sup> Commission Implementing Decision C(2013) 5934 final, granting, in exceptional circumstances, marketing authorisation under Regulation No 726/2004 for 'Orphacol (Cholic Acid)', an orphan medicinal product for human use.

<sup>121</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 10(1).

<sup>122</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 10(3)(b).

<sup>123</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 10(4).

<sup>124</sup> S. Borrás, C. Koutalakis & F. Wendler, 'European Agencies and Input Legitimacy: EFSA, EMeA and EPO in the Post-Delegation Phase', 29(5) *Journal of European Integration* (2007), pp. 583-600, p. 592f.

<sup>125</sup> Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers, OJ L 55, 28 February 2011, pp. 13-18.

<sup>126</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Arts. 13-14.

<sup>127</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 14(2).

<sup>128</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 14(3).

European Medicines Agency's. However, Member States also have a significant role in this process. This is through the CHMP whose members are representatives of competent authorities in the majority, appointed by the Member States, and through the involvement of Member States in the Standing Committee on Medicinal Products for Human Use, and their right to submit written observations to the Commission in the decision-drafting process.<sup>129</sup>

### 3.3.2 Decentralised and mutual recognition marketing authorisation procedures

As well as the centralised procedure and the national authorisation route, the decentralised and mutual recognition procedures provide for a marketing authorisation route where a medicinal product is supposed to be marketed in more than one Member State. The mutual recognition procedure and the decentralised procedure are laid down in the Community code relating to medicinal products (Directive 2001/83/EC).<sup>130</sup> Both the mutual recognition procedure and the decentralised procedure are of a hybrid nature, since the actual decision to authorise lies within the national system. The European level is only turned to as an arbitration mechanism.

The mutual recognition procedure foresees the authorisation in other Member States based on a marketing authorisation already granted in one Member State. This procedure is compulsory if a product with a marketing authorisation in one Member State is applied to be marketed in another Member State.<sup>131</sup> In the decentralised procedure, the product has not obtained a marketing authorisation in a Member State. The company first has to request a draft assessment report, a draft summary of product characteristics and a draft of the labelling and package leaflet from the regulatory authority of Member State of its choice.<sup>132</sup> While the two procedures follow the same scheme, the starting point of the procedures differs. In case of the mutual recognition procedure, the Member State where marketing authorisation has already been obtained becomes 'reference Member State' and has 90 days to update an existing marketing authorisation.<sup>133</sup> In case of the decentralised procedure, the Member State chosen by the company to start an authorisation procedure becomes the 'reference Member State', and has 120 days to draft a 'model decision' on a new marketing authorisation.<sup>134</sup>

The reference Member State then forwards its assessment to the other Member States where authorisation is sought (the concerned Member States). These concerned Member States then have 90 days to recognise the marketing approval decision of the reference Member State, including the summary of product characteristics, the labelling and the package leaflet.<sup>135</sup> They have 30 days to grant the national marketing authorisation.<sup>136</sup> In case

<sup>129</sup> Vos (1999), p. 223; Feick (2005), p. 13.

<sup>130</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 28-39. The decentralised procedure was introduced in 2004 through Directive 2004/27/EC of the European Parliament, and of the Council of 31 March 2004 amending Directive 2001/83/EC, on the Community code relating to medicinal products for human use, OJ L 136, 30 April 2004, pp. 34-57. In case a Member State realizes that a marketing authorisation is requested for a product that is already subject to marketing authorisation (or such procedure has started) in another Member State, according to Article 17(2) of Directive 2001/83/EC, the Member State concerned has to delay starting a marketing authorisation procedure, and point the applicant to the applicability of the mutual recognition or decentralised procedure.

<sup>131</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 28(2).

<sup>132</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 28(1) jo. 28(3).

<sup>133</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 28(2).

<sup>134</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 28(3).

<sup>135</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 28(4).

<sup>136</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 28(5).

a concerned Member State refuses to accept the assessment of the reference Member State for reasons of potential serious risk to public health, the matter will be referred to the Coordination Group for Mutual Recognition and Decentralized Procedures (CMDh),<sup>137</sup> where the Member States try to reach consensus and resolve differences in assessment.<sup>138</sup> If consensus is not found within 60 days, the matter will be referred to the EMA for arbitration.<sup>139</sup> Within the EMA, the CHMP will provide a scientific opinion on the matter. This scientific opinion is then forwarded to the Commission, which will adopt a decision that is binding upon the Member States, after consulting the Standing Committee on Pharmaceuticals under the examination procedure.<sup>140</sup>

The mutual recognition and decentralised procedures are thus characterised by three phases: (i) a national phase with reference and concerned Member States involved in a process of mutual recognition, (ii) an inter-administrative phase in the coordination group, and (iii) binding supranational arbitration in the EMA and the Commission.<sup>141</sup> It needs to be emphasised that the national phase of the procedure still remains the most important part, and that the intra-administrative and supranational phases only apply in case of disagreement between the Member States.

It remains to be concluded that medicinal products in the EU are regulated through an extensive framework of legislative and legally-binding Commission measures. The focus of this regulatory framework is the facilitation of the internal market: its core feature is the marketing authorisation requirement. This marketing authorisation can be obtained either in a purely national procedure, through decentralised/mutual recognition, or a centralised route. All of these procedures and the requirements to obtain a marketing authorisation are – in varying degrees – subject to European harmonisation. However, notwithstanding the current level of centralisation with supranational elements in the decentralised/mutual recognition procedure and a truly European centralised procedure, it is also worth noting that the national regulatory authorities are closely involved in both the centralised and decentralised marketing procedures on the European level.

#### 4. GOVERNING MEDICINAL PRODUCTS IN THE UNION THROUGH NON-LEGALLY BINDING MEASURES

The previous section has examined the complex and extensive legislative framework for pharmaceuticals in the European Union. However, this assessment would not be complete if it ignored the widespread use of non-binding measures adopted by the European

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<sup>137</sup> The CMDh is established according to Art. 27 of Directive 2001/83/EC and composed of one representative per Member State, with the Commission as observer. The CMDh does not form part of the EMA, however, its Secretariat is provided by the EMA.

<sup>138</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 29.

<sup>139</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 29(4).

<sup>140</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Arts. 32-34. In the context of the Lisbon Treaty the comitology procedure referred to in Directive 2001/83/EC, which was the management procedure according to Article 4 of the Comitology Decision (Council Decision 1999/468/EC laying down the procedures for the exercise of implementing powers conferred on the Commission, OJ L 184, 17 July 1999, pp. 23-26) has been replaced by the examination procedure as established in Article 5 of the new Comitology Regulation (Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers, OJ L 55, 28 February 2011, pp. 13-18).

<sup>141</sup> Feick (2005), p. 15f.

Commission and the European Medicines Agency to govern pharmaceuticals. Such 'post-legislative guidance' has become increasingly important in the regulation of complex risks and problems in the Union.<sup>142</sup> While the overarching lines of certain regulatory policies and often also the procedures necessary to execute them will be laid down in legislation, further details are increasingly provided for and elaborated on in guidance documents.

In the following, the non-binding measures governing pharmaceuticals in the form of Commission and EMA guidelines are further examined. The chapter will then conclude with an assessment of the legal nature of these guidelines under the 'soft law' concept. Besides providing a complete overview of the Union's regulatory framework for pharmaceuticals, the assessment of the use of non-binding measures on the European level is necessary. The global pharmaceutical standards that will be introduced in the next chapter are implemented into the regulatory framework of the EU through non-binding EMA guidelines and, as will be shown in chapter 5, can influence Commission guidelines. Thus, to provide for an understanding of the interplay of global pharmaceutical standards with EU pharmaceuticals regulation, an understanding of the non-binding measures governing pharmaceuticals in the EU is indispensable.

#### 4.1 *Non-binding measures governing pharmaceuticals: Administrative rule-making by the Commission and the EMA*

Non-binding measures have regulated pharmaceuticals in the EU since the early days of the harmonisation process. The Committee for Proprietary Medicinal Products, established by Council Directive 75/319/EEC,<sup>143</sup> formed working groups divided into quality, safety, biotechnology and efficacy, which advised the European Commission in the drafting of scientific guidelines.<sup>144</sup> These 'notes for guidance' clarified the required information and documentation to be compiled in a dossier for marketing authorisations, harmonising the national rules on these matters.<sup>145</sup> The harmonisation at that time was facilitated in the form of a Council Recommendation, which recommended that Member States 'ensure' that the medicinal products placed on the market complied with the 'notes for guidance' the recommendation contained in its Annex, and to base their evaluation and examination of marketing authorisation applications on this Annex.<sup>146</sup>

In order to accommodate the Member States, which were still responsible for the final marketing authorisation decisions and thus did not appreciate a legally-binding restriction of their freedom to assess the dossiers, a non-binding Council Recommendation incorporating

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<sup>142</sup> The literature on post-legislative guidance is particularly well-developed in the field of environmental law, see e.g.: J. Scott, 'In Legal Limbo: Post-Legislative Guidance as Challenge for Administrative Law', 48(2) *Common Market Law Review* (2011), pp. 329-355; E. Korkea-aho, 'Legal Interpretation of EU Framework Directives: A Soft Law Approach', 40(1) *European Law Review* (2015), pp. 70-88. See also: L. Senden, 'Soft Post-Legislative Rulemaking: A Time for More Stringent Control', 19(1) *European Law Journal* (2013), pp. 57-75.

<sup>143</sup> Second Council Directive 75/319/EEC, OJ L 147, 9 June 1975, pp. 13-22, Art. 8.

<sup>144</sup> F. Sauer, 'Preface', in J. van de Laan & J. DeGeorge (Eds.), *Global Approach in Safety Testing – ICH Guidelines Explained* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. v-viii, p. vi.

<sup>145</sup> Lisman & Lekkerkerker (2005), p. 75; National Institute for Public Health and the Environment, 'Minds Open – Sustainability of the European Regulatory System for Medicinal Products', RVIM-Report 2014-0033, p. 16.

<sup>146</sup> Council Recommendation 83/571/EEC of 26 October 1983 concerning tests relating to the placing on the market of proprietary medicinal products, OJ L 332, 28 November 1983, pp. 11-32.

the guidance drafted by the Commission together with the CPMP in its Annex was adopted.<sup>147</sup> The non-binding measure also responded to fears in the industry that binding provisions would result in a ‘race-to-the-top’, compiling the strictest national practices in a document, that would not allow for deviation.<sup>148</sup> The Commission has published the so-called ‘Notice to Applicants’ (NTA) since 1986, which provides guidance on marketing authorisation procedures and the presentation of the dossier.<sup>149</sup>

Overall such measures applicable to pharmaceuticals in the Union, laid down in non-binding measures, have augmented over time, leading to increasing detail in the harmonisation of regulatory requirements.<sup>150</sup> As will be shown in detail, the pharmaceutical standards regarding quality, safety and efficacy within the Union’s regulatory framework are placed in post-legislative guidance documents.<sup>151</sup> Nowadays, these non-binding measures are referred to as guidelines.<sup>152</sup> The EMA, taking the Commission’s position into account, has published the following definition of a guideline:

‘A *guideline* is a Community document with explicit legal basis referred to in the legislative framework as intended to fulfil a legal obligation laid down in the Community pharmaceutical legislation. It provides advice to applicants or marketing authorisation holders, competent authorities and/or other interested parties on the best and most appropriate way to fulfil an obligation laid down in the community pharmaceutical legislation.’<sup>153</sup>

As shown by this quote, these guidelines are addressed either to companies searching marketing authorisation or the national competent authorities having to assess the data submitted for marketing authorisation. In this respect, guidelines serve as tools for the clarification and substantiation of legislative requirements, working in favour of the regulated industry as well as of the public administration.<sup>154</sup>

The use of non-binding guidance allows for these documents to be updated according to scientific process or changing administrative requirements, without going through a laborious and time-consuming legislative amendment. Such guidelines are, thus, a type of administrative rule, intended to provide guidance on how legislative provisions, which are often rather general and non-concrete *qua* content, are translated into administrative practice.<sup>155</sup>

Today, with regard to the EU’s pharmaceutical regulation, the Commission and the European Medicines Agency share responsibility in publishing guidelines providing

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<sup>147</sup> Hancher (1989), p. 108.

<sup>148</sup> Ibidem.

<sup>149</sup> European Commission, Volume 2B – Notice to Applicants – Medicinal Products for Human Use, (Update May 2008), p. 2, available via: [http://ec.europa.eu/health/files/eudralex/vol-2/b/update\\_200805/ctd\\_05-2008\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-2/b/update_200805/ctd_05-2008_en.pdf), last accessed: 3 April 2017.

<sup>150</sup> Feick (2005), p. 21.

<sup>151</sup> Section 4.

<sup>152</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 5.

<sup>153</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 4, (emphasis in original document).

<sup>154</sup> I. Schneider, *Das Kooperationsprinzip im Vorfeld der Arzneimittelzulassung – Zum national und Europarechtlichen Rahmen des Zusammenwirken von Potentiellen Antragstellern und Zulassungsbehörden* (Frankfurt am Main: Peter Lang Europäischer Verlag der Wissenschaften, 2003), pp. 94-100.

<sup>155</sup> Hofmann, Rowe & Türk (2011), p. 537.

interpretation of pharmaceutical legislation, and guiding its application in practice. This task has been divided between the Commission and the EMA, according to the content of the guidelines. Commission guidelines usually address regulatory aspects such as the renewal of marketing authorisations, variations to marketing authorisations or package leaflet requirements.<sup>156</sup> The scientific EMA guidelines are concerned with defining the legislative requirements of quality, safety and efficacy.<sup>157</sup> In this sense, both Commission and EMA guidelines clarify legislative requirements and can be qualified as post-legislative guidance.

#### 4.1.1 Governing pharmaceuticals through post-legislative guidance: Commission guidelines

The guidelines drafted by the Commission are published on the Eudralex website it maintains.<sup>158</sup> This website comprises the so-called 'rules governing medicinal products in the European Union', which next to the basic pharmaceutical legislation (Volume 1 for human medicinal products, and Volume 5 for veterinary medicinal products), also comprises guidelines for both human and veterinary medicinal products. The latter will be disregarded since this research is only concerned with the regulation of human medicinal products. The most important post-legislative guidance in the EU's pharmaceutical regulation is the so-called 'Notice to Applicants' in Volume 2 of the rules governing medicinal products in the European Union. In Article 6(4) of Regulation (EC) 726/2004, the Commission has been mandated with 'drawing up a detailed guide regarding the form in which applications are to be presented' together with the EMA, the Member States and other interested parties. The Commission made use of this power by drafting an extensive collection of guidance documents.<sup>159</sup>

The Notice to Applicants is divided in three parts: one dealing with the procedures for marketing authorisation (Volume 2A), the second with the presentation and content of the dossier (Volume 2B), and the third containing so-called 'regulatory guidelines' (Volume 2C).

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<sup>156</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 6.

<sup>157</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 6.

<sup>158</sup> [http://ec.europa.eu/health/documents/eudralex/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/index_en.htm), last accessed: 3 April 2017.

<sup>159</sup> [http://ec.europa.eu/health/documents/eudralex/vol-2/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm), last accessed: 3 April 2017.

**Table 2: Commission guidelines governing pharmaceuticals**

| Commission guidelines governing pharmaceuticals<br>(as available in Eudralex on 11 March 2015 <sup>160</sup> ) |                   |
|--|-------------------|
| Volume 1 (Miscellaneous)   | 2 <sup>161</sup>  |
| Volume 2 A Notice to Applicants Marketing Authorisation  | 6 <sup>162</sup>  |
| Volume 2 B Notice to Applicants Presentation and content of the dossier  | 1                 |
| Volume 2C Notice to Applicants' Regulatory Guidelines  | 13                |
| Volume 4 Guidelines for good manufacturing practices for medicinal products for human and veterinary use       | 10 <sup>163</sup> |
| Volume 10 Guidelines for clinical trial  | 25 <sup>164</sup> |

The Notice to Applicants Volume 2A provides detailed guidance on marketing authorisation procedures in the Union and the institutional practices concerning this procedure, including clarification in the form of timelines. Volume 2B is concerned with the format of the marketing authorisation dossier, the Common Technical Document (CTD).<sup>165</sup> The Commission's regulatory guidelines compiled in Volume 2C address variations and renewals of marketing authorisations, changing the classification for the supply, or the readability of the labelling and package leaflet. They supplement the legislation where it does not provide for the definition of certain terms<sup>166</sup> or entail specifications of legislative requirements.<sup>167</sup> In

<sup>160</sup> This table was generated on the basis of the Eudralex website and reflects the status of the Commission guidelines on 11 March 2015. Outside the Eudralex, the Commission also adopted 3 guidelines in the field of orphan medicinal products. These can be found here: [http://ec.europa.eu/health/human-use/orphan-medicines/index\\_en.htm](http://ec.europa.eu/health/human-use/orphan-medicines/index_en.htm), last accessed: 3 April 2017.

<sup>161</sup> The website shows more guidelines, which are included in Volume 2. Moreover, the Miscellaneous part contains 4 Commission Communications who also have not been included.

<sup>162</sup> The Notice to Applicants is divided into Chapters, however it can be qualified as guidelines. (See: EMA, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 5.) Due to the extensive nature of the Chapters and the fact that they are drafted and updated separately, they have been counted as separate guidelines.

<sup>163</sup> Every Chapter was counted as a separate guideline. In addition, Volume 4 contains an introduction, a glossary and 19 Annexes.

<sup>164</sup> Volume 10 additionally contains a general information document and a variety of documents that have not been qualified as guidelines by the author, such as Q&A documents, annexes and lists of fields contained in the EudraCT database.

<sup>165</sup> See for further details on the CTD: Chapter 5, Section 3.2.

<sup>166</sup> The guidance on a new therapeutic indication for a well-established substance (November 2007) for example clarifies what a 'new indication' is. (European Commission, Guidance on a new Therapeutic Indication for a Well Established Substance, Brussels, November 2007). Another important example is the guideline on the definition of a potential serious risk to public health, which by defining 'potential serious risk' sets the delimitations for Member States to refuse a marketing authorisation in the mutual recognition and decentralised procedure. (European Commission, Guideline on the Definition of a Potential Serious Risk to Public Health in the context of Article 29(1) and (2) of Directive 2001/83/EC, OJ C 133, 8 June 2006, pp. 5-7).

<sup>167</sup> For example, the guideline on the readability of the labelling and package leaflet of medicinal products for human use provides *inter alia* for the font size that should be used for the package leaflet. (European Commission, Guideline on the Readability of the Labelling and Package

addition to Volume 2 of the Eudralex website, concerned with the marketing authorisation process in general, the special Volumes contain guidelines drafted by the Commission for good manufacturing practice (Volume 4) and clinical trials (Volume 10). In the past, the Commission was responsible for pharmacovigilance guidelines (Volume 9), which are now drafted by the EMA.<sup>168</sup>

Thus, the regulation of pharmaceuticals displays extensive use of non-binding administrative rules in the form of guidelines by the Commission, in order to supplement and clarify the legally binding measures applicable to pharmaceuticals in the Union. In contrast to the EMA scientific guidelines, which will be discussed below, the aim of the Commission guidelines is not to provide scientific details, but rather to describe and clarify applicable procedures in detail and define terminology used in the legislation.

#### 4.1.2 Governing pharmaceuticals through post-legislative guidance: EMA guidelines

The scientific guidelines drafted by the European Medicines Agency constitute Volume 3 of 'the rules governing medicinal products in the European Union', but they are now found on the website of the EMA, and not the Eudralex website provided for by the Commission.<sup>169</sup> The EMA's scientific committees adopt these guidelines. Most of them originate in the main scientific committee for human medicinal products, CHMP, but depending on the required field of expertise other committees might adopt them. The preparation of the guidelines might take place in standing or temporary working groups established by these committees.<sup>170</sup>

The EMA guidelines are drafted with the intention of harmonising the interpretation and application of the legislative requirements of quality, safety and efficacy, providing detailed guidance on these matters.<sup>171</sup> Moreover, they give guidance to marketing authorisation applicants on how the pharmaceutical product has to be tested during its development, and how an application needs to be substantiated by documentation.<sup>172</sup> These scientific guidelines represent 'a harmonised EU approach (...) based on the most up-to-date scientific knowledge'.<sup>173</sup> For example, the EMA has established a guideline on testing the carcinogenic potential – the potential of causing cancer – of medicinal products for human use.<sup>174</sup> This guideline defines how to conduct carcinogenicity studies in animals, providing specific details on the duration of the studies, the number of animals and the monitoring of

Leaflet of Medicinal Products for Human Use, ENTR/F/2/SF/jr (2009)D/869, 12 January 2009).

<sup>168</sup> The change was made in accordance with the 2010 pharmacovigilance legislation and is now reflected in Art. 108a of Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128.

<sup>169</sup> [www.ema.europa.eu](http://www.ema.europa.eu), last accessed: 3 April 2017.

<sup>170</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 56(2).

<sup>171</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 6. See also: S. Vamvakas, 'EU Perspectives on ICH', in J. van de Laan & J. DeGeorge (Eds.), *Global Approach in Safety Testing – ICH Guidelines Explained* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. 13-22, p. 16.

<sup>172</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 6.

<sup>173</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 4.

<sup>174</sup> Committee for Proprietary Medicinal Products (CPMP), Note for guidance on carcinogenic potential, CPMP/SWP/2877/00.

the study as well as the reporting of the study results. Other guidelines govern a specific category of medicinal products. For example, the guideline on medicinal products for the treatment of insomnia defines diagnostic criteria for insomnia and provides details on the assessment of the therapeutic efficacy of the medicinal product.<sup>175</sup>

Due to the rapidly changing scientific background of the criteria for marketing authorisation and the sheer amount of technical details necessary to define them for different products, these scientific requirements are not laid down in legislative measures, for which there is a long and cumbersome process for amendments, but in the form of guidelines.<sup>176</sup> In this sense, these guidelines constitute ‘voluntary expertise based rules, constituting measurable criteria by which a product or a production process or service can be evaluated on the basis of technical or physical conditions’, and can be qualified as standards under the definition established in Chapter 1.<sup>177</sup>

**Table 3: EMA guidelines governing pharmaceuticals**

| Scientific guidelines adopted by the EMA and its committees<br>(as available in Eudralex on 19 March 2015) |     |
|--|-----|
| Quality  | 57  |
| Biologicals  | 56  |
| Non-clinical   | 43  |
| Clinical efficacy and safety   | 125 |
| Multidisciplinary  | 49  |
| Other  | 7   |
| Total  | 337 |

With 337 scientific guidelines in force in March 2015, the European Medicines Agency has made extensive use of non-legally binding guidance documents. These guidelines form a large part of the regulatory framework of pharmaceuticals and are proof of an impressive level of detail governing the harmonisation of pharmaceutical regulation in the Union. Where the legislation spans the umbrella requirements of quality, safety and efficacy, it is the scientific guidance established by the experts in the scientific committees of the EMA that determines the application and interpretation of these requirements, and brings them to life with the scientific and technical standards.

#### 4.1.3 Interaction of legally-binding and non-binding measures in EU pharmaceutical regulation

As was shown before, the regulation of pharmaceuticals in the EU is characterised by an extensive legislative framework. These legislative measures interact with non-legislative but legally binding measures and a large amount of non-binding administrative rules in the form of guidelines, forming a complex regulatory structure governing pharmaceuticals in the Union. This interaction will be exemplified in the following through an examination of the rules and principles forming the Good Manufacturing Practice (GMP), which regulates the manufacturing process of medicinal products, addressing issues such as hygiene or documentation of the production.

<sup>175</sup> Committee for Medicinal Products for Human Use (CHMP), Guideline on medicinal products for the treatment of insomnia, EMA/CHMP/16274/2009. Insomnia is a sleep disorder.

<sup>176</sup> See also: Knauff (2010), p. 251f.

<sup>177</sup> Chapter 1, Section 2.2.

Along with the obligation to obtain marketing authorisation prior to the marketing of a medicinal product, the manufacturing of medicinal products is also subject to an authorisation requirement.<sup>178</sup> The manufacturing of medicinal products is regulated in Title IV 'Manufacture and Importation' of Directive 2001/83/EC. According to Article 46(f) of Directive 2001/83/EC, manufacturers are obliged to comply with the good manufacturing practice. However, the Directive does not specify what the GMP entails. Thus, Article 47 of Directive 2001/83/EC obliged the Commission to take several actions. Article 47 mandates the adoption of a directive to amend non-essential elements of Directive 2001/83/EC by supplementing it. This led to the adoption of Commission Directive 2003/94/EC providing the general rules of the good manufacturing practice.<sup>179</sup> Moreover, Article 47 of Directive 2001/83/EC mandates the adoption of delegated acts to establish principles and guidelines of good manufacturing practice for active substances.<sup>180</sup> Furthermore, it allows for the drafting of detailed guidelines by the Commission. These Commission guidelines are contained in Volume 4 of the Eudralex website, defining good manufacturing practice in accordance with the legislative requirements in detail.<sup>181</sup>

The interaction of these measures can be imagined like a cascade, where the general requirements are laid down in the legislative measure. These principles are then further established in a legally-binding Commission measure, and the regulatory details are laid down in non-binding guidelines. For example, Directive 2001/83/EC prescribes adherence to the good manufacturing practice. The core principles of this practice are laid down in Commission Directive 2003/94/EC, which *inter alia* establishes that 'manufacturers shall establish and implement an effective pharmaceutical quality assurance system'.<sup>182</sup> The requirements of such a pharmaceutical quality system are further specified in a Commission guideline.<sup>183</sup>

In general, a mix of several legally binding and non-binding forms of regulation is applied to regulate pharmaceuticals in the EU. The procedural, technical and scientific specificity of the measures increases as the legislative character of the measures decreases.

#### 4.2 *Pharmaceutical guidelines under review: legal nature in context of the EU soft law debate*

The preceding analysis has shown that non-binding measures form an essential part of the EU's pharmaceutical regulation. The growing influence of such measures in the EU raises

<sup>178</sup> Directive 2001/83/EC, OJ L 311, 28 November 2001, pp. 67-128, Art. 40.

<sup>179</sup> Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use, OJ L 262, 14 October 2003, pp. 22-26.

<sup>180</sup> On the basis of this provision, the Commission has adopted: Commission Delegated Regulation (EU) No 1252/2014 of 28 May 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council with regard to principles and guidelines of good manufacturing practice for active substances for medicinal products for human use (OJ L 337 25.11.2014), pp. 1-7.

<sup>181</sup> European Commission, Eudralex – The Rules Governing Medicinal Products in the European Union – Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use – Introduction, SANCO/C8/AM/sl/ares(2010)1064597, available via: [https://ec.europa.eu/health/documents/eudralex/vol-4\\_en](https://ec.europa.eu/health/documents/eudralex/vol-4_en), last accessed: 3 April 2017.

<sup>182</sup> Commission Directive 2003/94/EC, OJ L 262, 14 October 2003, pp. 22-26, Art. 6.

<sup>183</sup> European Commission, Eudralex – The Rules Governing Medicinal Products in the European Union – Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use – Chapter 1 Pharmaceutical Quality System, SANCO/AM/sl/ddg1.d.6(2012)860362.

the question of whether their identification as non-binding does accurately grasp their legal nature. As in Chapter 1, where the concept of soft law was used to assess the legal nature of global standards, the notion of soft law also lends itself to analysing non-binding measures in EU pharmaceutical regulation.<sup>184</sup>

While of course the governance framework and institutional actors differ from soft law in international law, in the EU context soft law is also understood to concern the determination of certain rules of conduct or policy directions, not in a legally binding instrument, but in a measure that irrespective of being devoid of legally binding power, does have practical and either direct or indirect legal effects.<sup>185</sup> The biggest difference between soft law in international law and soft law in European law is, however, that the EU (in contrast to most international organisations) does dispose of extensive power to adopt binding legislation and is, thus, not dependent on adopting soft law measures in order to regulate.<sup>186</sup>

Although the Treaties do not use the term ‘soft law’, apart from the recommendations and opinions mentioned in Article 288 TFEU, a large variety of measures used in the EU have been specified in literature as constituting soft law.<sup>187</sup> Examples of European instruments that can be qualified as soft law are ‘Green and White Papers, Council Conclusions, Joint Declarations, Council Resolutions, Codes of Conduct, guidelines, communications and recommendations’,<sup>188</sup> though this list is not exhaustive, as there is no established catalogue of soft law measures in the EU.

The term ‘soft law’ has been used frequently in the EU, especially in the debate surrounding EU new governance at the beginning of the 2000s.<sup>189</sup> The White Paper on European Governance in 2001 expressed that legislation is only part of the regulatory framework, and advocated a combination with non-legally binding measures, such as recommendations or guidelines, to achieve better regulation and facilitate faster reactions to changing market and scientific conditions.<sup>190</sup> Nonetheless, the phenomenon as such is not necessarily new, since the European integration process has from the very beginning relied on measures with unqualified legal status.<sup>191</sup> From the 1990s onwards, soft law was used extensively, for example in the area of competition law.<sup>192</sup>

In 1993, Francis Snyder pointed to the fact that soft law, and specifically ‘Commission

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<sup>184</sup> Chapter 1, Section 3.

<sup>185</sup> Senden (2003), p. 104.

<sup>186</sup> Knauff (2010), p. 296.

<sup>187</sup> An overview of different soft law measures in the EU is provided by Terpan (2015), pp. 68-96.

<sup>188</sup> European Parliament – Committee on Legal Affairs, Working Document on institutional and legal implications of the use of “soft law” instruments, Rapporteur: Manuel Medina Ortega, 14 February 2007, PE 384.581v02-00, p. 2.

<sup>189</sup> From the rich literature see e.g. D. Trubek, P. Cottrell & M. Nance, ‘Soft law’, ‘Hard law’ and European Integration’, in G. de Búrca & J. Scott (Eds.), *Law and New Governance in the EU and the US* (Oxford/Portland/Oregon: Hart Publishing, 2006), pp. 65-94; M. Dawson, *New Governance and the transformation of European Law: Coordinating EU Social Law and Policy* (Cambridge: Cambridge University Press, 2011b).

<sup>190</sup> European Commission, European Governance – A White Paper, COM(2001) 428 final, pp. 16-17.

<sup>191</sup> Examples are the European Commission notice on exclusive dealing constructs with commercial agents (OJ 139, 24 December 1962, p. 2921) and the European Commission notice on patent licensing agreements (OJ 139, 24 December 1962, p. 2922). See: Senden (2003), p. 3. See also: Peters & Pagotto (2006).

<sup>192</sup> M. Cini, ‘The Soft Law Approach: Commission Rule-making in the EU’s State Aid Regime’, 8(2) *Journal of European Public Policy* (2001), pp. 192-207; O. Ştefan, *Soft Law in Court: Competition Law, State Aid, and the Court of Justice of the European Union* (Alphen aan den Rijn: Kluwer, 2013).

soft law', forms an important part of the Community's rules, and that this importance is likely to grow due to the Commission's ever increasing administrative responsibility.<sup>193</sup> Today, this assumption can only be confirmed. Together with the Commission as the main source of European soft law,<sup>194</sup> European agencies like the EMA are increasingly becoming sources of administrative soft law.<sup>195</sup> Soft law in this administrative context is often used to increase legal certainty, in the sense that it adds more detail and explanation to an existing law.<sup>196</sup> These interpretative soft law measures are used to streamline the implementation of legislative measures, and inform those that have to apply the legislation, such as national authorities or regulated parties, on the details of the implementation. They can thus contribute to more transparency and uniformity in the implementation of a legislative measure.<sup>197</sup>

The Commission's competence to adopt soft law measures is based on specific provisions in primary or secondary law, or on its general competence to ensure the application of EU law enshrined in Article 17(1) TEU.<sup>198</sup> Where these measures lay down the way in which the Commission will exercise its discretion,<sup>199</sup> they can be attributed to the Commission's right to self-organisation.<sup>200</sup> With regard to the soft law adopted by European agencies, certain secondary legislative acts provide the power to adopt guidance documents to these agencies.<sup>201</sup> This practice is worth critical attention under the *Meroni* doctrine, which is interpreted as preventing the delegation of discretionary decision-making powers.<sup>202</sup>

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<sup>193</sup> F. Snyder, 'Soft Law and the Institutional Practice in the European Community', in S. Martin (Ed.), *The Construction of Europe – Essays in Order of Emile Noel* (Dordrecht: Kluwer, 1994), pp. 197-225, p. 200.

<sup>194</sup> Knauff (2010), p. 299.

<sup>195</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 8.

<sup>196</sup> J. Schwarze, 'Soft Law im Recht der Europäischen Union', 1 *Europarecht* (2011), pp. 3- 18, pp. 6-7; Hofmann, Rowe & Türk (2011), p. 536ff.

<sup>197</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 8.

<sup>198</sup> Examples of primary law provisions which grant the power for the adoption of Commission guidelines are Art. 156 TFEU in the area of social policy, Art. 168(2) TFEU in the area of public health, or Art. 181 TFEU in the area of research and technological development. See: Hofmann, Rowe & Türk (2011), p. 549; European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 22.

<sup>199</sup> The competence of the Commission to adopt such policy-defining guidelines has been confirmed by the Court, for example in a case concerning state aid (Case C-382/99 *Netherlands v. Commission* ECLI:EU:C:2002:363, para. 24).

<sup>200</sup> Hofmann, Rowe & Türk (2011), p. 570.

<sup>201</sup> As well as the legislation on pharmaceuticals, which will be elaborated below, the REACH Regulation is an example of secondary legislation, which provides for the adoption of guidance by the respective Agency, the European Chemicals Agency (ECHA). Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, p. 1-849.

<sup>202</sup> Case 9/56 *Meroni and Co., Industrie Metallurgiche S.p.A. v. Highly Authority*, ECLI:EU:C:1958:7; Case 10/56 *Meroni and Co., Industrie Metallurgiche S.p.A. v. Highly Authority*, ECLI:EU:C:1958:8. From the rich literature on the *Meroni* doctrine see: S. Griller & A. Orator, 'Everything under Control? The "Way Forward" for European Agencies in the Footsteps of the *Meroni*

However, since the soft law measures are – at least pro-forma – not legally binding, the current practice of agency administrative soft law is not deemed to contradict the Meroni doctrine, although it needs to be assessed critically where de facto agencies obtain policy-making powers.<sup>203</sup>

#### 4.2.1 Pharmaceutical guidelines as soft law

The concept of EU soft law acknowledges that non-legally binding measures can have (indirect) legal effects too. This section will therefore closely examine whether the guidelines drafted by the European Commission and the European Medicines Agency can also entail such (indirect) legal effects.

From a strictly legal perspective, guidelines do not constitute legally binding measures of EU law, as they are not amongst the legally binding instruments of the EU as enshrined in Article 288 TFEU. It is worth mentioning that the guidelines of the European Commission are published with a disclaimer. The website providing the Notice to Applicants explicitly states that the notice ‘has no legal force’ and that ‘(i)n case of doubt, therefore, reference should be made to the appropriate Union Directives and Regulations’.<sup>204</sup> This is also underlined by the European Medicines Agency’s guideline adoption procedure: ‘(w)ithin the framework of pharmaceutical legislation, guidelines do not have legal force and the definite legal requirements are those outlined in the relevant Community legislative framework (...) as well as appropriate national rules’.<sup>205</sup> Thus, the non-binding status of the guidelines is emphasised and communicated to the users of the guidelines.<sup>206</sup> The legislation will take priority over any guidelines. The content of the guidelines cannot contravene the rules laid down in the legislation, as was emphasised in an interview with officials of the Legal Department of the European Medicines Agency.<sup>207</sup>

At first glance the legal nature of guidelines adopted by the Commission and the European Medicines Agency is very clear. However, as discussed, the debate surrounding the soft law concept has shown it is worthwhile to look further than the strict binary qualification of legally binding and non-legally binding measures. In order to truly understand the legal nature of pharmaceutical guidelines, it is necessary to look beyond their

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Doctrine’, 35(1) *European Law Review* (2010), pp. 3-35; M. Chamon, ‘EU Agencies in between Meroni and Romano or the Devil and the Deep Blue Sea’, 48(4) *Common Market Law Review* (2011), pp. 1055-1075.

<sup>203</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 23.

<sup>204</sup> [http://ec.europa.eu/health/documents/eudralex/vol-2/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm), last accessed: 3 April 2017. A similar disclaimer is also found in Chapter 1 of The Notice Applicants.

<sup>205</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 4.

<sup>206</sup> For the sake of completeness, it should be mentioned here that one guideline has acquired legally binding force. This concerns the ‘Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMEA/410/01 Rev. 2 – October 2003), adopted by the Committee for Proprietary Medicinal Products (CPMP) and by the Committee for Veterinary Medicinal Products (CVMP)’. Adherence to the note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents has been made obligatory through Annex 1 of Directive 2001/83/EC (see Annex 1 at 3.2(9), 3.2.1.2(c) and 3.2.2.4(c)). The note explicitly states that it ‘has been given the force of law’.

<sup>207</sup> Interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

formal status and the disclaimers towards the potential legal effects – direct or indirect – and practical effects these instruments are prompting. Such effects might for example be caused by their interaction with legally binding measures applicable to pharmaceuticals.<sup>208</sup> It is essential to assess the reinforcement of the guidelines through legislation and their function as an interpreting tool to further qualify legislative requirements.

The guidelines drafted by the EMA and the Commission are reinforced through legislation. According to Article 8(3) of Directive 2001/83/EC, a marketing authorisation application needs to be submitted in the specific format and containing the documents that are enlisted in Annex 1 of the Directive. Annex 1 to Directive 2001/83/EC under (1) sets out that the application shall follow the format set out in the Notice to Applicants, in Volume 2B. It also sets out under (4) in the Annex that in assembling the dossier, the applicant shall take the guidelines published by the EMA and the Commission into account. In order to harmonise the requirements of the marketing authorisation, this Annex is not only referred to in the Directive which governs decentralised and national procedures, but also Article 6(1) of Regulation (EC) 726/2004, which regulates the centralised procedures and requires the application of Annex 1 of the Directive. Thus, although not legally binding, through reinforcement by the Regulation and the Directive, they have to be taken into account both in the centralised and decentralised/mutual recognition European marketing authorisation procedures as well as in national procedures – with and without a European element. The guidelines do not become binding, but the reference in the legislation certainly fortifies their significance in marketing authorisation applications.

Apart from the obligation to take the guidelines into account, the legal relevance of guidelines is strengthened through legislation where guidelines are adopted on an explicit legal basis, as is clarified by the definition of guidelines by the EMA.<sup>209</sup> An example for guidelines adopted on an explicit legal basis are the Commission guidelines in Volume 4 of the Eudralex website, defining the good manufacturing practice in detail, adopted based on Article 47 of Directive 2001/83/EC.<sup>210</sup> Examples of legal mandates for the EMA to adopt guidelines are to be found in Annex 1 of Directive 2001/83/EC. Annex 1 under Part I 4.2.3. Toxicology provides that the duration of repeat-dose toxicity testing is defined in EMA guidelines, which provides a basis for the adoption of repeat-dose toxicity guidelines by the Agency.

For the sake of completeness it should be mentioned that before the EMA adopted the definition of a guideline in 2009, the term 'guideline' was also more loosely used to include other documents 'considered to provide advice to applicants or marketing authorisation holders, competent authorities, and/or other interested parties on the best or most appropriate way to fulfill an obligation laid down in the community pharmaceutical legislation'.<sup>211</sup> However, for those guidelines with a clear legal basis, the EMA's procedure for guideline adoption is very instructive as the document qualifies the guidelines as 'soft law'. Furthermore, it emphasises that in cases where a guideline adopted by the Commission

<sup>208</sup> Hofmann, Rowe & Türk (2011), p. 552. They explain that although formally measure may be non-binding, this effect may be achieved indirectly.

<sup>209</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 4.

<sup>210</sup> European Commission, Eudralex – The Rules Governing Medicinal Products in the European Union – Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use – Introduction, SANCO/C8/AM/sl/ares(2010)1064597.

<sup>211</sup> European Medicines Agency, Status of EMEA Scientific Guidelines and European Pharmacopoeia Monographs and chapters in the regulatory framework applicable to medicinal products, 11 September 2008, EMEA/42371/2008 – corr, p. 2.

or the EMA serves as clarification of a legal obligation, it can become ‘quasi-binding’ through this legal basis.<sup>212</sup> Additionally, the interview with two officials of the EMA’s Legal Department confirmed that the guidelines with an explicit legal basis could be considered more binding than the ones without a basis in the legislation.<sup>213</sup>

Thus, although the guidelines are not legally binding, through Annex 1 of Directive 2001/83/EC, they have to be taken into account in the process of assembling the marketing authorisation dossier. Moreover, where they are adopted with a clear basis in legislation they are of ‘quasi-binding’ nature. The following will provide further insight into the direct and indirect legal effects that the guidelines adopted by the Commission and the EMA can have on three actors: (i) the marketing authorisation applicants, (ii) the Member States, and (iii) the Commission and the EMA themselves, in order to examine the potential soft law nature of the guidelines.

#### 4.2.2 Effect of guidelines on the marketing authorisation applicant

The first dimension of a potential soft law nature of guidelines, is the legal effect of guidelines on the marketing authorisation applicants, which will be considered in the following section. As established, the guidelines drafted by the EMA and the Commission are reinforced through legislation by Article 8(3) of Directive 2001/83/EC, in conjunction with Annex 1 to Directive 2001/83/EC as well as Article 6(1) of Regulation (EC) 726/2004. Therefore, a marketing authorisation applicant needs to take the guidelines of both the Commission and the EMA into account when submitting an application.

As the Commission guidelines usually address regulatory aspects – including matters such as the renewal of marketing authorisations, variations to marketing authorisations, or packaging requirements, they serve to clarify and ensure compliance with legislative requirements.<sup>214</sup> For example, Commission guidelines address the labelling and packaging requirements that a product is subjected to in detail according to Articles 8(3)(j), 57, 60, 62 and 65(f) of Directive 2001/83/EC.<sup>215</sup> As these regulatory matters are presented as further clarification of legislative requirements, it is questionable whether there is indeed room for the applicant to deviate from the guidelines.

With regard to the EMA’s scientific guidelines, a more in-depth analysis of their effect on the marketing authorisation applicant is required. The EMA’s clarification of the legal status of these guidelines provides that if regulators and marketing authorisation applicants adhere to these guidelines this ‘will facilitate assessment, approval and control of medicinal products in the European Union’.<sup>216</sup> Adherence to the guidelines is thus presented as the route to enable the assessment of the application. In essence, the guidelines regulate which

<sup>212</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 4.

<sup>213</sup> Interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>214</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 6.

<sup>215</sup> European Commission, Guideline on the Packaging Information of Medicinal Products for Human Use Authorised by the Union, July 2015, Revision 14.3, available via: [http://ec.europa.eu/health/files/eudralex/vol-2/2015-07\\_14\\_3\\_packaging.pdf](http://ec.europa.eu/health/files/eudralex/vol-2/2015-07_14_3_packaging.pdf), last accessed: 3 April 2017.

<sup>216</sup> European Medicines Agency, Status of EMEA Scientific Guidelines and European Pharmacopoeia Monographs and chapters in the regulatory framework applicable to medicinal products, 11 September 2008, EMEA/42371/2008 – corr, p. 2.

scientific evidence has to be provided by the marketing authorisation applicant in the dossier and, thereby, establish the basis for the assessment of the marketing authorisation application by the scientific committee. Therefore, they provide the applicants with the information on which standards are acceptable from a scientific point of view to prove the quality, safety and efficacy of a medicinal product.<sup>217</sup>

Moreover, the EMA states that where guidelines are adopted but have not yet entered into effect, applicants may already follow such guidelines, while 'competent authorities should wait until this period has expired before requiring the guideline to be taken into account'.<sup>218</sup> Given the non-binding character of the guidelines, the choice of the word 'requiring' is interesting, as it indicates that the leeway given to decide not to apply the guidelines might be smaller than their non-binding character might suggest. Indeed on the agency's website, the message regarding the status of guidelines is firm: '(t)he Agency *strongly encourages* applicants and marketing-authorisation holders to follow these guidelines. Applicants *need to justify deviations* from guidelines fully in their applications at the time of submission'.<sup>219</sup>

Undoubtedly, not all scientific questions for every product can be regulated in these guidelines. The science in the guidelines is certainly not set in stone and deviation is possible if justified.<sup>220</sup> Overall, the compliance with the guidelines – provided that the result of the prescribed tests confirm what is sought to be proven – creates a presumption of conformity with the legislative requirements of quality, safety and efficacy, whereas deviations from guidelines have to be duly justified,<sup>221</sup> and this can be a deterrent.

Where applicants deviate from the scientific guidelines they face a shifted burden of proof with regard to compliance with legislative requirements: a presumption of conformity lies in the adherence to standards, while deviation requires the extra step of its justification by the applicant.<sup>222</sup> Given that some of the guidelines would already have to be taken into account in the research and development process of the product, there would be a risk of not being able to justify a deviation from the guidelines come the end of a long and highly expensive process. It is possible for companies to request scientific advice from the EMA on the appropriate test to demonstrate the quality, safety and efficacy of medicinal products.<sup>223</sup> However, this advice is not legally binding on the agency in an ensuing authorisation procedure and a fee must be paid.<sup>224</sup> In an interview with an official of the European Federation of Pharmaceutical Industries and Associations (EFPIA), it was confirmed that

<sup>217</sup> Interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>218</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 13.

<sup>219</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000043.jsp&mid=WC0b01ac05800240cb](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000043.jsp&mid=WC0b01ac05800240cb), (emphasis added), last accessed: 3 April 2017.

<sup>220</sup> Interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>221</sup> European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr, 18 March 2009, p. 5.

<sup>222</sup> I am thankful to Elise Muir for pointing this out to me. See also: Scott (2004), p. 314.

<sup>223</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 57(1)(n).

<sup>224</sup> European Medicines Agency, Guidance for applicants seeking scientific advice and protocol assistance, EMA/691788/2010 Rev. 7, 19 September 2014; European Medicines Agency, Explanatory Note on the fees payable to the European Medicines Agency, EMA/800328/2013, 20 March 2014.

companies in practice usually follow the guidelines, rather than to try to justify a deviation from the guidelines.<sup>225</sup>

Overall, although both the Commission and EMA guidelines are non-binding measures, it has to be concluded that their application to marketing authorisation requests is compelling. The fact that they present, on the one hand, the Commission's clarification of core regulatory requirements and, on the other hand, the scientific standard to prove the legislative requirements of quality, safety and efficacy as accepted by the EMA, means that they indirectly become binding where deviation cannot be justified.

#### 4.2.3 Effect of guidelines on Member States

Another dimension of the 'quasi-binding' nature of these guidelines is their effect on the Member States. Although this research limits itself to the role of global standards at the EU level, it is worth mentioning that the guidelines are not only directed to applicants explicitly but also to regulatory authorities in the Member States.

It should be noted that national procedures underlie the European harmonisation through Directive 2001/83/EC, as Articles 6 and 8 require the application of Annex 1. Therefore, the guidelines formed on the European level, both by the Commission and the EMA, also work through to purely national authorisation procedures.<sup>226</sup> However, some of the guidelines will not apply to the Member States, where the products covered in the guidelines by their very nature are subject to the centralised procedure under Regulation (EC) 726/2004 and therefore are not covered by the national procedures.<sup>227</sup>

In general, European administrative guidelines are very influential on the Member States. A study by Senden and van den Brink shows that guidelines serving as a soft law guidance measure will have an effect on the national legislator transposing European law, and also on the national administration applying the respective legislation, as well as on the judiciary in the Member States.<sup>228</sup> All of these national actors will look for guidance on the interpretation of EU legislation in non-binding guidelines. This effect of non-binding measures on national courts has been recognised in the *Grimaldi* case, as the Court of Justice obliged national courts to take a non-binding recommendation into account, where they rule on disputes which require an interpretation of EU law.<sup>229</sup> Therefore, although not legally binding, guidelines do establish practical guidance for various actors in the Member States to comply with EU law.<sup>230</sup>

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<sup>225</sup> Interview with an official of the European Federation of Pharmaceutical Industries and Associations (EFPIA), conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>226</sup> In an interview with an official of the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), the German national authority with competence, it was confirmed that European soft law rules form an important part of national pharmaceutical regulation. Interview with an official of the BfArM, conducted in Bonn on 26 February 2015, notes on file with the author.

<sup>227</sup> Interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>228</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 8.

<sup>229</sup> Case C-322/88 *Salvatore Grimaldi v. Fonds des Maladies Professionnelles*, ECLI:EU:C:1989:646, para. 18.

<sup>230</sup> Hofmann, Rowe & Türk (2011), p. 569.

## 4.2.4 Effect of guidelines on the Commission and EMA

A third dimension of the direct or indirect legal effect of guidelines has to be considered for the authors – the Commission and the EMA – themselves, as administrative rules can be ‘self-binding’ upon the body that publishes them.<sup>231</sup> In general, the Court of Justice of the European Union has followed the principle that, provided the soft law instruments are compatible with the Treaties, an institution may not deviate from the guidelines it has adopted.<sup>232</sup> Thus, guidelines considerably limit the discretion of the authoring institution and impose a duty of compliance.<sup>233</sup> The Court argued for a self-binding effect of soft law measures on the basis of general principles of law such as equal treatment, legitimate expectations and legal certainty.<sup>234</sup> Thus, these administrative rules might generate legal effects.<sup>235</sup>

With regard to the specific case of pharmaceuticals, a clear-cut answer cannot be provided as, according to the knowledge of the author, a deviation of the EMA from its own guidelines has never been subject to a public debate or judicial review. However, especially in staff cases and competition law cases surrounding the question of self-binding effect of guidance document, the self-binding power of soft law, allowing only for deviation where this is duly reasoned, has been established.<sup>236</sup> Although these rules are developed in specific regulatory areas and their application in other areas of regulation is not clear,<sup>237</sup> it is difficult to argue why the same principles of equal treatment, legitimate expectations, and legal certainty would not apply in the field of pharmaceuticals. In the regulation of pharmaceuticals, the publication of the very detailed guidelines should also give rise to legitimate expectations. Applicants that adjust the very expensive and long enduring development process of their medicinal products should be protected by equal treatment and legal certainty.

To conclude, although the guidelines adopted by the Commission and EMA are labelled as non-binding instruments, they are powerful regulatory tools with considerable practical and at times indirect legal effects on individuals, Member States, and also the EU bodies themselves, where they publish such measures. The freedom to deviate from the

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<sup>231</sup> Schwarze (2011), p. 8.

<sup>232</sup> See: Case C-382/99 *Netherlands v. Commission*, ECLI:EU:C:2002:363, para. 24; Case C-313/90 *Comité International de la Rayonne et des Fibres Synthétique (CIRFS) and Others v. Commission*, ECLI:EU:C:1993:111, paras. 34 and 36; Case C-311/94 *IJssel-Vliet Combinatie v. Minister van Economische Zaken*, ECLI:EU:C:1996:383, para. 42; Case T-214/95 *Vlaamse Gewest v. Commission*, ECLI:EU:T:1998:77, para. 79.

<sup>233</sup> Joined cases C-189, 202, 205, 208 and 213/02P *Dansk Rørindustri and others v. Commission*, ECLI:EU:C:2005:408, para. 211. See also: A. Simonati, ‘The Principles of Administrative Procedure and the EU Courts: An Evolution in Progress?’, 4(1) *Review of European Administrative Law* (2011), pp. 45-81, p. 58; O. Ştefan, ‘European Union Soft Law: New Developments Concerning the Divide Between Legally Binding Force and Legal Effects’, 75(5) *The Modern Law Review* (2012), pp. 865-893, p. 882.

<sup>234</sup> Joined cases C-189, 202, 205, 208 and 213/02P *Dansk Rørindustri and others v. Commission*, ECLI:EU:C:2005:408, para. 211; Case T-73/04 *Carbone-Lorraine v. Commission*, ECLI:EU:T:2008:416, para. 71. See also: Hofmann, Rowe & Türk (2011), p. 567; O. Ştefan, ‘Helping Loose Ends Meet? The Judicial Acknowledgement of Soft Law as a Tool of Multi-Level Governance’, 21(2) *Maastricht Journal of European and Comparative Law* (2014), pp. 359-378, p. 367f.

<sup>235</sup> Joined cases C-189, 202, 205, 208 and 213/02P *Dansk Rørindustri and others v. Commission*, ECLI:EU:C:2005:408, para. 211.

<sup>236</sup> Senden (2003), pp. 415-458; Ştefan (2014), pp. 359-378.

<sup>237</sup> Hofmann, Rowe & Türk (2011), p. 568.

guidelines for all these actors is heavily restricted and their non-binding nature only superficially disguises this. Therefore, these guidelines constitute soft law, being adopted in the form of a legally non-binding instrument, but even though they are devoid of legally binding power, they have practical and (indirect) legal effects.<sup>238</sup>

## 5. CONCLUSION

This chapter has shown that the history of harmonisation in the pharmaceuticals field in the European Union is a history of incremental integration. This begins with a request for marketing authorisation based on an assessment of quality, safety and efficacy, and then gradually filling this requirement with harmonised technical and scientific details. Until today, there has been no unified European procedure for marketing authorisation. Applicants can either apply for purely national authorisation, can take the route of a decentralised or mutual recognition authorisation procedure, or can apply for a centralised marketing authorisation. The procedural route depends on the type of medicinal product and the question of where the product should be marketed. Thus, different types of pharmaceuticals are subject to diverging degrees of harmonisation and ‘institutional layering’<sup>239</sup> of authorisation procedures involving different actors. Although marketing authorisations have been increasingly Europeanised over the course of time, the Member States have retained considerable influence. Indeed, even in the centralised procedure the Member States – through the members they nominate for the scientific committees of the EMA – still play an important role.

After more than 50 years of European pharmaceutical regulation, the legislative framework covering pharmaceuticals extensively regulates the marketing authorisation of medicinal products. Rules about labelling, advertising and the wholesale of pharmaceuticals are governed by EU legislation. This legislative framework has been supported by an institutional structure consisting of the European Commission and the European Medicines Agency as key actors. The European Medicines Agency has established itself as a central figure in the marketing authorisation procedure, and forms the core of a large network of national regulatory authorities.

As well as the legally binding measures this chapter has established the essential role of non-binding administrative rule-making in the EU’s pharmaceutical regulation. The Commission has adopted a large variety of regulatory guidelines including the extensive ‘Notice to applicants’, which explains the practicalities of marketing authorisation procedures in detail. The European Medicines Agency also maintains a considerable amount of guidelines, which fill the legislative requirements of quality, safety and efficacy with life through the establishment of scientific and technical norms. It was established that regardless of their non-binding character, the guidelines adopted by the Commission and the EMA can be qualified as soft law, due to their considerable indirect legal and practical effects on the marketing authorisation applicants, the Member States, and themselves as authors of these guidelines. These guidelines, therefore, form an important part of the EU pharmaceutical regulatory framework. As the next chapter will show, pharmaceutical standards adopted on the global level are implemented into the regulatory framework of the EU through their adoption as EMA guidelines.

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<sup>238</sup> Senden (2003), p. 104.

<sup>239</sup> Feick (2005), p. 19.

## Chapter 4: The International Council for Harmonisation (ICH) – Institutional framework and standard-setting

### 1. INTRODUCTION

While the regulation of access to pharmaceutical markets used to be ‘virtually synonymous with national sovereignty’,<sup>1</sup> being closely linked to the administrative and socio-economic culture of a state,<sup>2</sup> the pharmaceutical sector serves as a good example for the growing harmonisation of regulatory requirements on the international level due to globalisation of trade. Nowadays, standards for pharmaceuticals are set globally, and the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH)<sup>3</sup> forms a very important source of pharmaceutical standards as a ‘leading platform for global pharmaceutical regulatory harmonisation’.<sup>4</sup>

The creation of the International Conference on Harmonisation, renamed in 2015 in line with its institutional reform as the International Council for Harmonisation,<sup>5</sup> was a response to the increasing globalisation of pharmaceutical trade, leading to a market structure where producing, manufacturing and marketing of medicines takes place in separate countries.<sup>6</sup> This internationalisation of the pharmaceutical business meant that effective regulation of pharmaceuticals could not remain a purely national task, as observed by Hancher as early as 1989, shortly before the inception of the ICH.<sup>7</sup>

This chapter will introduce the ICH with regard to its history, membership, mandate and funding (Section 2). It will analyse the ICH in terms of its institutional structure (Section 3), the standard-setting process operated in the ICH (Section 4), and legal nature of the ICH (Section 5). Furthermore, the chapter will examine the standards set by the ICH (Section 6), including an analysis of the legal nature of ICH guidelines (Section 6.2).

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<sup>1</sup> D. Vogel, ‘The Globalization of Pharmaceutical Regulation’, 11(1) *Governance* (1998), pp. 1-22, p. 1. See also: D. Kidd, ‘The International Conference on Harmonization of Pharmaceutical Regulations, the European Medicines Evaluation Agency, and the FDA: Who’s Zooming Who?’, 4(1) *Indiana Journal of Global Legal Studies* (1996), pp. 183-206, p. 203.

<sup>2</sup> Spina (2011), p. 250.

<sup>3</sup> The ICH used to be called International Conference on Harmonisation of Pharmaceuticals for Human Use and was renamed in 2015 in line with its institutional reform, which will be discussed in detail in this chapter.

<sup>4</sup> ICH, Press Release – ICH announces organisational changes as it marks 25 years of successful harmonisation, Geneva, 26 October 2015, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/News\\_room/B-Press\\_Releases/-Press\\_Release\\_26Oct2015\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/News_room/B-Press_Releases/-Press_Release_26Oct2015_Final.pdf), last accessed: 3 April 2017.

<sup>5</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_Articles\\_of\\_Association\\_for\\_Assembly\\_final\\_9Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_Articles_of_Association_for_Assembly_final_9Nov2016.pdf), last accessed: 3 April 2017.

<sup>6</sup> R. Kanusky, ‘Pharmaceutical Harmonization: Standardizing Regulations among the United States, the European Economic Community, and Japan’, 16(3) *Houston Journal of International Law* (1994), pp. 665-707, p. 667.

<sup>7</sup> Hancher (1989), p. 22.

## 2. THE ICH – HISTORY, MEMBERSHIP, MANDATE AND FUNDING OF THE HARMONISATION INITIATIVE

Today, the ICH significantly influences the regulatory requirements for pharmaceutical products around the globe; over the course of its existence, its institutional structure has evolved to reflect the increase of importance of its standards for pharmaceutical regulation globally. This section will introduce the history of this body, and address the reform process that the ICH launched in 2012. Moreover, the membership of the ICH pre- and post-reform will be examined. Finally, the ICH mandate will be scrutinized and its funding will be subjected to closer assessment.

### 2.1 History

The movement towards the global harmonisation of pharmaceutical standards is based on both economic factors, including the lowering of costs for manufacturers to comply with diverging regulatory schemes, and regulatory factors, such as increasing the speed of marketing authorisations and prevention of unnecessary duplicate trials.<sup>8</sup> For example, some countries like the US required clinical trials delivering the obligatory data for a marketing authorisation to be carried out in their own country.<sup>9</sup> Thus, clinical trials for the same medicine had to be carried out in several countries, whenever a product was to be marketed in multiple countries. Moreover, before the harmonisation of registration requirements, enormous costs were generated through obligatory marketing authorisation applications. These often encompassed thousands of pages, for every individual country, with content that had to be adjusted laboriously, requiring different trials.<sup>10</sup> This was extremely cost intensive; in the United States the cost of drug development had risen from an average of 50 million dollars in the 1970s to over 230 million dollars in the 1990s with the increasing regulatory requirements.<sup>11</sup> These figures only cover the marketing in one country and multiplied where the pharmaceutical product was marketed in more countries, leading to extremely high development costs for pharmaceuticals. Martin Bangemann, then Vice-President of the European Commission expressed in his opening speech at the 1<sup>st</sup> International Conference on Harmonisation that the money spent on adapting the dossiers for the respective regulators would be better used for innovative research and the development of new medicinal products.<sup>12</sup>

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<sup>8</sup> In this regard, the ICH has published two information brochures: ICH, 'The Value and Benefits of ICH for Industry', January 2000, available via: <http://www.ich.org/ichnews/publications/browse/article/the-values-and-benefits-of-ich-to-industry.html>, last accessed: 3 April 2017; ICH, 'The Value and Benefits of ICH to Drug Regulatory Authorities', November 2010, available via: <http://www.ich.org/ichnews/publications/browse/article/the-value-and-benefits-of-ich-to-drug-regulatory-authorities.html>, last accessed: 3 April 2017. See also: A. Berman, 'The Public-Private Nature of Harmonisation Networks', (2011) CTEI Working Paper, CTEI-2011-06, p. 13.

<sup>9</sup> Vogel (1998), p. 1-22, p. 9.

<sup>10</sup> B. Kuhnert, 'ICH at 20: An overview', 3(2) *Drug Information Association Global Forum* (2011), pp. 17-18, p. 18.

<sup>11</sup> D. Jordan, 'International Regulatory Harmonization: A new Era in Prescription Drug Approval', 25(3) *Vanderbilt Journal of Transnational Law* (1992), pp. 471-507, p. 484.

<sup>12</sup> M. Bangemann, 'Welcome Address by Mr Martin Bangemann', in P. D'Arcy & D. Harron (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992), pp. 1-5, p. 4. Bangemann said: 'Research costs money and a successful outcome of this conference would release funds currently spent on repeated

However, also the rise of the EU as a regulatory power and the problems concerning excessive time loss in the authorisation process by the US Food and Drug Administration (FDA) in the 1980s paved the way for harmonised regulatory standards for quality, safety and efficacy of medicinal products.<sup>13</sup> Until the 1990s, the US Food and Drug Administration dominated the regulation of medicinal products, determining the standards applicable to quality, safety and efficacy, not only for the US but also globally due to its large regulatory impact.<sup>14</sup> Nonetheless, the US faced a severe crisis in medication approval in the 1980s, with products taking over 10 years to be authorised for use on the US market. This even led to protests by AIDS activists at the FDA premises in 1988.<sup>15</sup> The FDA regulatory process had slowed down due to the detailed regulation and the need to assess more information, while the European process had sped up, leading to shorter approval times in the EU.<sup>16</sup>

Indeed, with the progress of the European harmonisation process, the FDA had to face the fact that the EU had severely gained in regulatory capacity through centralisation, institutional reforms and coordination of regulation amongst the Member States.<sup>17</sup> The harmonisation process led to an increasing influence of the EU and its Member States, now speaking with one voice, on the development of regulatory practices in the field of pharmaceuticals. Besides the US, the EU too became an important actor in pharmaceutical regulation, leading to greater diversity in regulatory requirements. The regulatory authorities had a strong interest in cooperation in order to benefit from each other's experience. Moreover, the pharmaceutical industry at the time also strongly advocated harmonising the technical and scientific requirements for marketing authorisations.<sup>18</sup>

These developments paved the way for the start of an unprecedented harmonisation initiative in the field of pharmaceuticals – the ICH. The catalyst to forming the ICH was a sequence of bilateral and trilateral negotiations between EU, US and Japanese regulators which formed the largest markets for the development of research-based medicines.<sup>19</sup> The US and Japan had been working together since the mid-1980s on the opening up of the Japanese markets, also leading to some degree of harmonisation within their pharmaceutical regulation.<sup>20</sup> In 1988, the EU and Japan also addressed problems arising from diverging pharmaceutical regulations, such as unnecessary double-testing, and for a longer period

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'defensive' research, and allow saved resources towards the development of new medicines through 'innovative' research, for the direct benefit of patients and consumers.'

<sup>13</sup> Vogel (2012), pp. 189-202; Berman (2011a), p. 13.

<sup>14</sup> D. Bach & A. Newman, 'Governing Lipitor and Listerine: The Domestic Roots of International Pharmaceutical and Cosmetics Regulation', IE Business School Working Paper, WP08-17, (11 March 2008), p. 4.

<sup>15</sup> Jordan (1992), p. 473.

<sup>16</sup> F. Rockhold, 'Industry Perspectives on ICH Guidelines', 21(19) *Statistics in Medicine* (2002), pp. 2949-2957, p. 2950.

<sup>17</sup> Bach & Newman (2008), p. 4.

<sup>18</sup> O. Doi, 'Role and Public Health Responsibilities of the Authorities', in P. D'Arcy & D. Harron (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992), pp. 18-26, p. 20.

<sup>19</sup> Jordan (1992), p. 492. The research-based pharmaceutical industry is engaged in the innovation of medicinal products, marketing products developed on the basis of their own research, in contrast to manufacturers of generics, which are bioequivalent to existent products.

<sup>20</sup> R. Arnold, 'Objectives and Preparation of the Conference and the Role of the Workshops', in P. D'Arcy & D. Harron (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992), pp. 7-11, p. 8.

between the development of a drug and its actual marketing.<sup>21</sup> During the same period, a subcommittee of the European Commission dealing with medicines legislation and marketing authorisation, the so-called Discussion Group III, organised a conference with representatives from the US Food and Drug Administration (FDA), and the Ministry of Health and Welfare in Japan (MHW, today MHLW for Ministry of Health, Labour and Welfare).<sup>22</sup>

These regulatory talks evolved into plans to form a harmonisation initiative between the three regulatory authorities. Concrete plans for action were finally agreed at the 1989 WHO Conference of Drug Regulatory Authorities (ICDRA) in Paris, where representatives of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) and representatives of the regulatory authorities met.<sup>23</sup> In April 1990, the European Federation of Pharmaceutical Industries and Associations (EFPIA) in Brussels hosted a meeting with representatives from the three regulatory authorities and industry associations of the research-based pharmaceutical industry. Dr. Sauer (European Commission), Dr. Baudrihaye (EFPIA), Dr. Shirota (Japan Pharmaceutical Manufacturers Association, JPMA), Dr. Doi (MHW), Prof. Alexandre (CPMP),<sup>24</sup> Dr. Esber (FDA) and A. Giaquinto (Pharmaceutical Research and Manufacturers of America, PhRMA), outlining concrete plans for the ICH.<sup>25</sup> This meeting marks the ‘date of birth’ of the ICH.<sup>26</sup>

Following from these discussions, the first meeting of the Steering Committee forming the main governing body of the ICH took place in April 1990 in Brussels, chaired by Dr. Sauer.<sup>27</sup> At this meeting the ‘Terms of Reference’ setting out the ICH mandate was agreed upon, as well as the separation of harmonisation topics into safety, quality and efficacy.<sup>28</sup> In addition to that, it was agreed to conduct the harmonisation through large-scale conferences, where an extensive range of experts could discuss future guidelines.<sup>29</sup> It was decided to organise the initial ICH Conference in 1991 in Brussels, harmonising the first aspects of drug regulation, especially with regard to testing requirements.<sup>30</sup> For the preparation of this Conference three further Steering Committee meetings were held, each accompanied by

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<sup>21</sup> P. Bahri & P. Tsintis, ‘Pharmacovigilance-related topics at the level of the International Conference on Harmonisation (ICH)’, 14(6) *Pharmacoepidemiology and Drug Safety* (2005), pp. 377-387, p. 378.

<sup>22</sup> J. Contrera, ‘The Food and Drug Administration and the International Conference on Harmonisation: How Harmonious Will International Pharmaceutical Regulations Become?’, 8(4) *The Administrative Law Journal* (1994-1995), pp. 927-960, p. 939.

<sup>23</sup> *Ibidem*.

<sup>24</sup> At that time the Committee for Proprietary Medicinal Products (CPMP) was a scientific expert advisory committee to the European Commission. See further: Chapter 3, Section 2.

<sup>25</sup> F. Augier de Crémiers, ‘The Birth of ICH E3 and How it Led to the CTD’, 3(2) *Drug Information Association Global Forum* (2011), pp. 19-20, p. 19; Sauer (2013), pp. v-viii, p. vii. See also: <http://www.ich.org/about/history.html>, last accessed: 3 April 2017.

<sup>26</sup> ‘The birth of ICH took place at a meeting in April 1990, hosted by EFPIA in Brussels. Representatives of the regulatory agencies and industry associations of Europe, Japan and the US met, primarily, to plan an International Conference but the meeting also discussed the wider implications and terms of reference of ICH.’, via: <http://www.ich.org/about/history.html>, last accessed: 3 April 2017.

<sup>27</sup> Sauer (2013), pp. v-viii, p. vii.

<sup>28</sup> <http://www.ich.org/about/history.html>, last accessed: 3 April 2017.

<sup>29</sup> Sauer (2013), pp. v-viii, p. vii.

<sup>30</sup> Abraham & Reed (2001), p. 114; D. Katsikas, ‘International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceutical Products’, in T. Hale & D. Held (Eds.), *Handbook of Transnational Governance – Institutions & Innovations* (Cambridge: Polity Press, 2011), pp. 88-94, p. 89.

meetings of Expert Working Groups on the topics of quality, safety and efficacy preparing the scientific discussions for the first ICH Conference.<sup>31</sup> The first ICH Conference took place in Brussels in 1991, with over 1,000 participants from the regulatory authorities and industry associations of the EU, US and Japan but also other regulatory authorities from all over the world, paving the way for regulatory and industry cooperation to form common standards.<sup>32</sup>

The standards developed, the ICH guidelines were not only successful with regard to implementation by the regulators: in the early days of harmonisation through the ICH, the pharmaceutical industry used these guidelines immediately. By 1996, 90% of pharmaceutical companies were using existing ICH quality guidelines, with the largest companies almost entirely following suit.<sup>33</sup> The ICH is of exemplary importance in the area of global risk regulation standards, not only because of the impact of its standards in the European and global context, but also because in the politically sensitive field of pharmaceuticals, it was the first initiative to bring a group of national regulators together in one harmonisation forum. The involvement of industry in such a body was a novelty in terms of pharmaceutical regulation.<sup>34</sup>

It is noteworthy that with the creation of the ICH, the parties did not follow the route of setting up a harmonisation initiative within the framework of the WHO, to which the three ICH regulator authorities are also parties<sup>35</sup> Instead they established an independent initiative of their own, disregarding the fact that the WHO as an international organisation of the United Nations presumably enjoys higher legitimacy under international law,<sup>36</sup> and has a mandate in standard-setting for pharmaceutical products.<sup>37</sup> Berman suggests several reasons for the choice of stepping outside the WHO framework.<sup>38</sup> Firstly, the aim of the parties to involve private actors in the initiative would not have been feasible within the WHO, due to its intergovernmentalist nature.<sup>39</sup> Secondly, a large majority of WHO member countries were simply not hosting a strong research-based pharmaceutical industry.<sup>40</sup> Finally, the creation of the ICH was a step towards more efficiency as processes in the WHO were regarded as too slow and bureaucratic.<sup>41</sup> This also follows from a speech from the Executive Vice President of the IFPMA at the first ICH Conference, who stated that reaching consensus in global harmonisation processes would be too cumbersome.<sup>42</sup>

Thus, the ICH was set up as a regionally limited initiative between the regulators and industry associations representing the research-based pharmaceutical industry of the US, EU and Japan, independent from existing international harmonisation initiatives. Moreover, the ICH was not established as an international organisation but as an informal, meeting based process. And nor was the ICH's institutional structure established in a founding document. While the veterinary equivalent of the ICH, the VICH, has an organisational charter, the

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<sup>31</sup> Sauer (2013), pp. v-viii, p. viii.

<sup>32</sup> Bangemann (1992), p. 1.

<sup>33</sup> Vogel (1998), p. 13.

<sup>34</sup> Berman (2011a), p. 3.

<sup>35</sup> Nonetheless, it is worth mentioning that the WHO has attended the ICH Steering Committee meetings as observer since the establishment of the ICH, ensuring an institutional link between the WHO and the ICH. See further: Section 2.2.3.

<sup>36</sup> Dagron (2012) p. 16.

<sup>37</sup> WHO, Constitution of the World Health Organisation, 22 July 1946, Art. 2(u).

<sup>38</sup> Berman (2011a).

<sup>39</sup> Berman (2011a), p. 17.

<sup>40</sup> Berman (2011a), p. 15.

<sup>41</sup> Berman (2011a), p. 16.

<sup>42</sup> Arnold (1992), p. 8.

ICH had no document laying down its mandate, institutional structure and the like.<sup>43</sup> It only had ‘Terms of Reference’, which provided an overview of the ICH’s mandate but did not contain information on the ICH as organisation.<sup>44</sup>

From 1991 until 2003 the Steering Committee, forming the ICH’s main decision-making body, and the Expert Working Groups, which are the scientific expert bodies for the respective harmonisation topics, met in six monthly intervals. Moreover, the parties conducted international conferences every two to three years where representatives of the six sponsors were gathering, as a distinguishable characteristic of the ICH harmonisation process.<sup>45</sup> The ICH Conferences were conducted on a large scale with over a thousand participants invited for the first Conference, to discuss the topics prepared by the Steering Committee together with the working groups.<sup>46</sup> Since its inception the ICH has convened in a large-scale international conference format six times: 1991 in Brussels (Belgium), 1993 in Orlando (USA), 1995 in Yokohama (Japan), 1997 in Brussels (Belgium) again, in 2000 in San Diego (USA), and the last time being the ICH6 in November 2003, taking place in Osaka (Japan).<sup>47</sup>

The large-scale conference format was abolished in the Steering Committee meeting of May 2007 taking place in Brussels.<sup>48</sup> It was replaced with Steering Committee and Expert Working Group meetings twice a year during the so-called ‘ICH week’. This renewed meeting format was deemed to enable ‘more frequent and more focused’ work within the ICH.<sup>49</sup> Furthermore, the ICH decided to conduct so-called ICH Public Events at the end of the Steering Committee meetings, or as specifically organised regional meetings.<sup>50</sup> These Public Events aimed at the communication of ICH activities and also took the form of preparatory meetings, where the participants commented on topics that will be discussed in the next Steering Committee and Expert Working Group Meetings.

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<sup>43</sup> International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), Organisational Charter of VICH, VICH/96/002 Revision 13, October 2016 FINAL.

<sup>44</sup> ICH, The Future of ICH – Revised 2000 – Statement by the ICH Steering Committee on the occasion of the Fifth International Conference on Harmonisation, 9-11 November 2000, San Diego, p. 2 available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/-Vision/The\\_Future\\_of\\_ICH\\_-\\_Revised\\_2000.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/-Vision/The_Future_of_ICH_-_Revised_2000.pdf), last accessed: 6 May 2015 (the information has now been removed from the website. A copy is on file with the author).

<sup>45</sup> J. Lee, ‘What is Past is Prologue: The International Conference on Harmonization and Lessons Learned from European Drug Regulations Harmonization’, 26(1) *University of Pennsylvania Journal of International Economic Law* (2005), pp. 151-191, p. 179.

<sup>46</sup> Sauer (2013), pp. v-viii, p. vii.

<sup>47</sup> ICH, Proceedings of the ICH Tokyo Symposium: Hot Topics and Influence on Asia – Tokyo 2007, p. 1, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/E-ICH\\_Public\\_Meetings/ICH\\_Symposium\\_Tokyo\\_Japan\\_Nov\\_2\\_2007/Tokyo\\_-\\_Symposium\\_Proceedings\\_2007.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/E-ICH_Public_Meetings/ICH_Symposium_Tokyo_Japan_Nov_2_2007/Tokyo_-_Symposium_Proceedings_2007.pdf), last accessed: 3 April 2017.

<sup>48</sup> ICH, ICH Steering Committee May 5-10, 2007, Brussels, Belgium – Summary, p. 8, available via: [http://www.ich.org/fileadmin/\\_migrated/content\\_uploads/SC\\_Report\\_Brussels\\_2007-.pdf](http://www.ich.org/fileadmin/_migrated/content_uploads/SC_Report_Brussels_2007-.pdf), last accessed: 3 April 2017.

<sup>49</sup> ICH, ICH Steering Committee May 5-10, 2007, Brussels, Belgium – Summary, p. 8, available via: [http://www.ich.org/fileadmin/\\_migrated/content\\_uploads/SC\\_Report\\_Brussels\\_2007-.pdf](http://www.ich.org/fileadmin/_migrated/content_uploads/SC_Report_Brussels_2007-.pdf), last accessed: 3 April 2017.

<sup>50</sup> For an overview see: <http://www.ich.org/meetings/ich-public-events.html>, last accessed: 3 April 2017.

### 2.1.1 ICH as a global standard-setter and reflection of this development in its institutional structure

The first decade of ICH work was mostly devoted to harmonising the quality, safety and efficacy requirements of the three founding regions through the development of ICH guidelines. However, in a second phase, the ICH gradually entered into communicating its activities to non-ICH regulators.<sup>51</sup> The WHO played a prominent role. As observer in the ICH process, the WHO shared information about ICH work with its non-ICH member countries.<sup>52</sup> The impact of ICH guidelines on non-ICH countries was well recognised by 2002: they were used as references or educational materials, for example for seminars conducted in the regional harmonisation efforts of the Association of Southeast Asian Nations (ASEAN).<sup>53</sup> Nonetheless, although the ICH guidelines were also implemented in non-ICH countries, regulatory authorities of other countries were not granted membership in the ICH until the recent reform.

In response to the increasing influence of ICH standards beyond the founding regions, the ICH created the Global Cooperation Group (GCP) in 1999. The GCP used to be a sub-committee of the Steering Committee and was composed of one representative of each ICH Steering Committee member as well as one representative per observer and one representative of the ICH Secretariat.<sup>54</sup> The group published information materials and held presentations on the ICH.<sup>55</sup> In 2003, the ICH opened the GCP to the participation of 'Permanent Representatives' from non-ICH and Regional Harmonisation Initiatives (RHIs), provided that these initiatives were actively undertaking a scientific harmonisation of regulatory requirements in their region.<sup>56</sup> In 2008, the GCP also welcomed members of Drug Regulatory Authorities (DRAs) or Departments of Health (DoHs) for the first time, thus not regional initiatives but national regulators of countries such as Australia, Chinese Taipei, Singapore and South Korea.<sup>57</sup> As of June 2013, the Global Cooperation Group was abolished and the topics formerly covered by this group were integrated as a standing item

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<sup>51</sup> This statement can be found on the ICH website: 'Since ICH's inception in 1990, the ICH process has gradually evolved. ICH's first decade saw significant progress in the development of ICH Guidelines on Safety, Quality and Efficacy topics. Work was also undertaken on a number of important multidisciplinary topics, which included MedDRA (Medical Dictionary for Regulatory Activities) and the CTD (Common Technical Document). As ICH started into a new millennium, the need to expand communication and dissemination of information on ICH Guidelines with non-ICH regions became a key focus. Attention was also directed throughout the second decade towards facilitating the implementation of ICH Guidelines in ICH's own regions and maintaining already existing ICH Guidelines as science and technology continued to evolve.', available via: <http://www.ich.org/about/history.html>, last accessed: 3 April 2017.

<sup>52</sup> ICH, *The Future of ICH – Revised 2000*, Statement by the ICH Steering Committee on the occasion of the Fifth International Conference on Harmonisation, 9-11 November 2000, San Diego, p. 2 (the information has now been removed from the website. A copy is on file with the author).

<sup>53</sup> WHO, 'The Impact of Implementation of ICH Guidelines in Non-ICH Countries', Regulatory Support Series No. 009, 2002, p. 15.

<sup>54</sup> ICH, *ICH Global Cooperation Group – Terms of Reference*, November 2003, p.1, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Vision/GCG\\_Statement\\_2003.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Vision/GCG_Statement_2003.pdf), last accessed: 3 April 2017.

<sup>55</sup> ICH, *ICH Global Cooperation Group – Terms of Reference*, November 2003, p. 1.

<sup>56</sup> ICH, *ICH Global Cooperation Group – Terms of Reference*, November 2003, p. 1.

<sup>57</sup> ICH, *ICH Global Cooperation Group Meeting Report*, Tuesday June 3, 2008, Portland, Oregon, USA, p. 2, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/C-GCG\\_Reports/June\\_2008\\_Portland\\_USA/Final\\_GCG\\_Report\\_Portland\\_USA\\_June\\_2008.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/C-GCG_Reports/June_2008_Portland_USA/Final_GCG_Report_Portland_USA_June_2008.pdf), last accessed: 3 April 2017.

on the Steering Committee Meeting Agenda to facilitate a better involvement of the global regulators.<sup>58</sup>

Besides the Global Cooperation, the so-called Regulators Forum met for the first time in Portland in June 2008. This included the regulatory ICH parties as well as regulators of other countries which had implemented ICH guidelines, such as Australia, Chinese Taipei, Singapore and South Korea. Regulators of countries vital to the production of pharmaceuticals and the carrying out of clinical trials, such as Brazil, China, India and Russia, were also involved.<sup>59</sup> The purpose of the Regulators Forum was declared to be the exchange of best practices regarding the implementation of ICH guidelines. It was also to create a forum for discussion amongst regulators of the impact of ICH guidelines on the regulatory system of non-ICH countries.<sup>60</sup> Although the forum still meets in conjunction with the ICH week and continues to discuss the implementation of ICH guidelines, the forum obtained a more formal status – removed from the ICH’s institutional structure – as the International Pharmaceutical Regulators Forum (IPRF) in 2013.<sup>61</sup>

Progressively the ICH’s institutional structure was modified to open up to the increasing involvement of non-ICH member industrial organisations, regional harmonisation initiatives and regulatory authorities. However, as much as the non-ICH countries and regions were supported in the implementation of ICH guidelines, they remained merely recipients of the guidelines. Although the international acceptance of ICH guidelines was proof of the influence the ICH has on global harmonisation, the development of the guidelines was problematic. Other countries were not represented as full members within the ICH, lacking voting rights in the adoption of the guidelines. The use of ICH guidelines as pharmaceutical standards, in the regulatory frameworks of non-ICH members too, raised doubts with regard to their legitimate role as globally dominant reference points in pharmaceuticals regulation, due to the lack of inclusiveness.<sup>62</sup> This was criticised in particular because ICH members were leading in the advancement of technology within the pharmaceutical field. Developing countries faced difficulties in enforcing these high standards without endangering their own industrial or public health policies.<sup>63</sup>

### 2.1.2 ICH Reform

Since the SC meeting in Fukuoka in June 2012, the ICH has been working on new principles of governance. This effort concerned the redefinition of the roles of regulators and industry parties with the aim of increasing of transparency in ICH processes.<sup>64</sup> These developments will be discussed later in this chapter. However, these procedural changes soon extended

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<sup>58</sup> ICH, ICH Steering Committee, La Hulpe, Belgium, June 2013, Press Release, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-la-hulpe-belgium-june-2013.html>, last accessed: 3 April 2017.

<sup>59</sup> ICH, ‘The Value and Benefits of ICH to Drug Regulatory Authorities’, November 2010, p. 20.

<sup>60</sup> ICH, ‘The Value and Benefits of ICH to Drug Regulatory Authorities’, November 2010, p. 20.

<sup>61</sup> See: <https://www.i-p-r-f.org/en/>, last accessed: 3 April 2017.

<sup>62</sup> Dagron (2012).

<sup>63</sup> WHO, ‘The Impact of Implementation of ICH Guidelines in Non-ICH Countries’, Regulatory Support Series No. 009, 2002, p. 19ff, A. Berman, ‘The Distributional Effects of Transnational Pharmaceutical Regulation’, (2012a) CTEI Working Paper, CTEI-2012-01.

<sup>64</sup> ICH, Press Release – ICH Steering Committee, Fukuoka, Japan, 6-7 June 2012, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-fukuoka-japan-6-7-june-2012.html>, last accessed: 3 April 2017.

into a reform that concerned the institutional structure of the ICH, with special attention to an improved exchange with global regulators.<sup>65</sup>

The reform process was triggered by several factors. One factor was the dependence on the IFPMA to conclude contracts for the ICH, including the hosting of the secretariat, which is caused by the lack of legal personality of the ICH.<sup>66</sup> Moreover, the Commission officials also stated in the interviews conducted for this research that one of the core ideas behind the reform process was to make the ICH more regulator-driven, and to have ICH membership reflect the national regulators and international industry associations actually affected by the guidelines.<sup>67</sup>

Central points of the reform were declared to be the broadening of membership (with regard to regulators and industry organisations<sup>68</sup>), the clarification of the distinct roles of industry and regulators, the establishment of a new legal entity and a change in the funding of the ICH.<sup>69</sup> Through this reform the ICH seeks to establish itself as the focal point for global pharmaceutical regulatory harmonisation, involving the key global and regulatory actors, while keeping the harmonisation process efficient.

The organisational reform started taking shape in December 2014.<sup>70</sup> At the ICH Inaugural Assembly on 23 October 2015 the ICH Founding Members adopted the Articles of Association, which established the ICH as an association under Article 60 et seq of the Swiss Civil Code, and introduced 'International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use' as the official name of the association.<sup>71</sup> With regard to its legal establishment, a Swiss association was chosen, as this form of legal personality is highly flexible in terms of membership criteria, the process for adding members and leaving the association, as well as adopting a funding framework.<sup>72</sup> Moreover,

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<sup>65</sup> ICH, Press Release – ICH Steering Committee, San Diego, USA, 14-15 November 2012, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-fukuoka-japan-6-7-june-2012.html>, last accessed: 3 April 2017.

<sup>66</sup> European Commission, 70th meeting of the Pharmaceutical Committee, 27 March 2013, PHARM 621, International developments – Agenda Item 5a) Information from the Commission on the Reform of the ICH and the Regulators Forum, p. 2, available via: <https://ec.europa.eu/health/sites/health/files/files/committee/70meeting/pharm621.pdf>, last accessed: 3 April 2017.

<sup>67</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>68</sup> ICH, Press Release – ICH Steering Committee, Osaka, Japan November 2013, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-osaka-japan-november-2013.html>, last accessed: 3 April 2017.

<sup>69</sup> ICH, Press Release – ICH Steering Committee, Minneapolis, MN, USA, June 2014, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-minneapolis-mn-usa-june-2014.html>, last accessed: 3 April 2017.

<sup>70</sup> ICH, Press Release – ICH Steering Committee, Lisbon, Portugal, December 2014, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-lisbon-portugal-november-2014.html>, last accessed: 3 April 2017.

<sup>71</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 1.

<sup>72</sup> European Commission, 70th meeting of the Pharmaceutical Committee, 27 March 2013, PHARM 621, International developments – Agenda Item 5a) Information from the Commission on the Reform of the ICH and the Regulators Forum, p. 2. Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

since the Secretariat was already located in Geneva, this ensured continuity and simplified the transition process.<sup>73</sup>

## 2.2 Membership

From its inception until 2014, the ICH only granted full membership to regulators and industry representatives of the US, EU and Japan. The current reform has substantially modified the membership structure, leading to the creation of several membership categories, with varying prerogatives.

### 2.2.1 ICH Membership pre-reform

It has been pointed out that the ICH developed as a regional initiative amongst the US, the EU and Japan. At the time of the ICH establishment, they represented the largest pharmaceutical markets of the world, with 75 % of pharmaceuticals produced in these regions and 90 % of research and development taking place there.<sup>74</sup> Looking at more recent numbers from the year 2016, with regard to new medicines with active ingredients marketed for the first time between 2001 and 2015, these three regions account for the largest share in sales.<sup>75</sup> Hence, from the outset ICH membership was subject to regional limitations according to market size in terms of pharmaceuticals.

Thus, the members founding the ICH were representatives from regulatory authorities and research-based pharmaceutical industry associations of the three largest drug markets in the world:

- the European Commission together with the European Medicines Agency (EMA), since the EMA was established in 1993;
- the Ministry of Health, Labour and Welfare (MHLW) from Japan, supported by the Pharmaceuticals and Medical Devices Agency (PMDA);
- the US Food and Drug Administration (FDA);
- European Federation of Pharmaceutical Industries and Associations (EFPIA);
- the Japan Pharmaceutical Manufacturers Association (JPMA); and
- the Pharmaceutical Research and Manufacturers of America (PhRMA).

ICH membership remained limited to these regions for most of its operational history.

However, in June 2014, the regulatory authority of Switzerland (Swissmedic) and the Health Products and Food Branch (HPFB) of the Canadian authority Health Canada became members of the Steering Committee, which formed the main governing body of the ICH before the reform.<sup>76</sup> Before that, they had observer status since the inception of the ICH in 1990, giving them the right to attend meetings but not to take part in the decision-making. Swissmedic previously represented the European Free Trade Association (EFTA) as

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<sup>73</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>74</sup> Jordan (1992), p. 492.

<sup>75</sup> EFPIA, 'The Pharmaceutical Industry in Figures – Key Data 2016', p.4, available via: <http://www.efpia.eu/uploads/Modules/Documents/the-pharmaceutical-industry-in-figures-2016.pdf>, accessed: 3 April 2017.

<sup>76</sup> ICH, Press Release – ICH Steering Committee, Minneapolis, MN, USA, June 2014.

an observer in the ICH process.<sup>77</sup> The change in status was recognition of the long-term active contribution of these two parties to the ICH process and their commitment to implementing the ICH guidelines.<sup>78</sup> Moreover, this was the first step in the institutional reform process of the ICH.<sup>79</sup>

### 2.2.2 ICH Membership post-reform

Through the recent reform process, the membership structure of the ICH has been subject to fundamental changes. The new Articles of Association, which were adopted at the ICH Inaugural Assembly on 23 October 2015 and approved by the Assembly on 9 November 2016, introduces five different categories of membership:

- Founding Regulatory Members,
- Founding Industry Members,
- Standing Regulatory Members,
- Regulatory Members, and
- Industry Members.<sup>80</sup>

Attached to the different categories of membership are specific rights and duties, as the membership shapes the institutional role and influence in the decision-making process in the ICH, details of which will be explained in the analysis of the institutional structure of the ICH.<sup>81</sup>

In principle, the six original ICH members still maintain a special status, as they are now Founding Regulatory Members or Founding Industry Members. Thus, the Founding Regulatory Member status is confined to the European Commission, the Ministry of Health, Labour and Welfare of Japan (MHLW) (also represented by the Pharmaceuticals and Medical Devices Agency (PMDA)), and the US Food and Drug Administration (FDA).<sup>82</sup> The Founding Industry Member status is limited to the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Japan Pharmaceuticals Manufacturers Association (JPMA), and the Pharmaceutical Research and Manufacturers of

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<sup>77</sup> Nowadays, the EFTA countries do not formally take part in the ICH. However, the other EFTA countries Iceland, Norway and Liechtenstein are already applying the EU regulation of pharmaceuticals as parties to the European Economic Area (EEA). Decision of the EEA Joint Committee N74/1999 of 28 May 1999 amending Protocol 37 and Annex II (technical regulations, standards, testing and certification) to the EEA Agreement, OJ L 284, 09.11.2000, pp. 65-70.

<sup>78</sup> International Conference on Harmonisation Press Release – ICH Steering Committee, Minneapolis, MN, USA, June 2014.

<sup>79</sup> International Conference on Harmonisation Press Release – ICH Steering Committee, Minneapolis, MN, USA, June 2014.

<sup>80</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 7-12.

<sup>81</sup> Section 3.

<sup>82</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 8.

America (PhRMA).<sup>83</sup>

From an EU perspective it is remarkable that the European Commission is mentioned as a Founding Regulatory Member. In the past, while acknowledgement of the membership in an official document was lacking, the website of the ICH stated:

‘The ICH Parties are comprised of representatives from the following Regulatory Parties:

- European Union, the Regulatory Party is represented by the European Commission (EC) and the European Medicines Agency (EMA) (...)’<sup>84</sup>

Thus, before the reform, the EU was presented as a member represented by the European Commission and the EMA. Therefore, the change in the Articles of Association means that on an ICH level, the EMA is no longer formally mentioned as a member. Instead, the focus has shifted from the EU being a member, to the European Commission being a member. This seems to be due to a shift in emphasis in the structure of the ICH from certain regions as members, to granting membership to regulatory authorities responsible for the regulation of pharmaceutical products for human use.

From an EU law perspective, this is of course also relevant for the question of whether the Commission is competent to be a member of the ICH as a Swiss Association. In this regard, it is important to establish that the ICH was not founded through a binding international agreement. In principle, the Swiss Association is founded by the adoption of the Articles of Association in accordance with Article 60 of the Swiss Civil Code.<sup>85</sup> There is no binding international agreement between the respective members that would create the ICH. However, in the context of the ICH reform process, the Commission adopted a decision, establishing its participation as Founding Regulatory Member in the ICH and approving the ICH Articles of Association.<sup>86</sup>

The general framework for the Commission’s participation in global standard-setting bodies was discussed in Chapter 1, where it was established that in cases of standard-setting bodies that are not international organisations, the Commission takes part in the setting of standards on the basis of its EU internal regulatory competences, while it has to respect the policy-making power of the Council.<sup>87</sup> In this regard, the preamble of the Commission Decision on the participation of the Commission in the ICH is instructive:

‘(6) The Commission’s primary responsibility in the pharmaceutical sector is to propose legislation, ensure compliance with existing legislation, and to develop policy. The work of the ICH assists in the development of Union policy in this field. The activities of ICH are purely technical and scientific as the purpose is to agree on common scientific and technical standards relating to medicinal products for human use in the form of non-

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<sup>83</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 9.

<sup>84</sup> <http://www.ich.org/about/faqs.html>, last accessed: 24 February 2016 (the information has now been removed from the website. A copy is on file with the author).

<sup>85</sup> Swiss Civil Code of 10 December 1907, Status as of 1 January 2017.

<sup>86</sup> European Commission, Commission Decision C(2015) 7256 final of 23 October 2015 on the participation of the Commission as Founding Regulatory Member in the ‘International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use’. This decision is not in the public domain but has been obtained through an access to documents request. A copy is on file with the author.

<sup>87</sup> See Chapter 1, Section 5.1.

binding ICH guidelines. The technical and scientific collaboration in the ICH Association thus complements Union policy and legislation in this field.<sup>88</sup>

The membership of the Commission in the ICH is thus a natural extension of its internal regulatory function and does not distort the institutional balance, as the ICH guidelines do not legally bind the EU, and are of a non-political nature.<sup>89</sup>

It is remarkable that in Article 8 of the Articles of Association about the Founding Regulatory Members, the Japanese Pharmaceuticals and Medical Devices Agency is listed as being able to represent the Japanese Ministry of Health, Labour and Welfare of Japan, whereas the EMA is not even mentioned. This might, however be due to the fact that the EMA cannot represent the Commission in the ICH because of the allocation of competences in European institutional law; it will merely continue to support the Commission. This interpretation is supported by the fact that the summary record of the Pharmaceutical Committee of the Commission from October 2015 with regard to the ICH Reform states that: ‘The Commission, as a founding member of ICH, will continue, with the support of the European Medicines Agency (EMA), to play a leading role in the further development of ICH activities.’<sup>90</sup> The Rules of Procedure of the ICH Assembly also mention that the delegation of the European Commission will include EMA representatives.<sup>91</sup> In the preamble, the Commission’s Decision on the Commission participation in the ICH states that the ‘EMA should continue to support the Commission by having ongoing involvement in the ICH Association, if requested by the Commission, and this support is fully in line with Regulation (EC) No 726/2004 on the establishment of the EMA’.<sup>92</sup> Thus, although the EMA is not formally acknowledged within the ICH, from an EU perspective it carries out important supporting functions upon request of the Commission, based on the mandate contained in its founding regulation, as discussed in Chapter 1.<sup>93</sup>

Besides the Founding Regulatory and Industry Members, the ICH reform introduced the category of Standing Regulatory Members. This category covers legislative or administrative authorities, which are responsible for regulating pharmaceutical products for

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<sup>88</sup> European Commission, Commission Decision C(2015) 7256 final of 23 October 2015 on the participation of the Commission as Founding Regulatory Member in the ‘International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use’. This decision is not in the public domain but has been obtained through an access to documents request. A copy is on file with the author.

<sup>89</sup> See Chapter 1, Section 5.1.

<sup>90</sup> European Commission, 75th meeting of the Pharmaceutical Committee, 21 October 2015, PHARM 701, Summary Record, p. 10, available via: [https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pharm701\\_summary\\_record.pdf](https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pharm701_summary_record.pdf), last accessed: 3 April 2017.

<sup>91</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 7, available via: [http://www.ich.org/fileadmin/-Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_Assembly\\_RoPs\\_Approved\\_by\\_Assembly\\_final\\_9Nov2016.pdf](http://www.ich.org/fileadmin/-Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_Assembly_RoPs_Approved_by_Assembly_final_9Nov2016.pdf), last accessed: 3 April 2017.

<sup>92</sup> European Commission, Commission Decision C(2015) 7256 final of 23 October 2015 on the participation of the Commission as Founding Regulatory Member in the ‘International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use’, Preamble 8. This decision is not in the public domain but has been obtained through an access to documents request. A copy is on file with the author.

<sup>93</sup> Chapter 1, Section 5.2.

human use and have been a member of the Steering Committee of the ICH before its establishment as association.<sup>94</sup> This type of membership is restricted in fact to only Swissmedic and Health Canada, which became members of the Steering Committee in 2014 and were not ICH founding members.<sup>95</sup> Indeed, the minutes of the Inaugural Assembly confirm that both Swissmedic and Health Canada have been approved as Standing Regulatory Members.<sup>96</sup>

Consequently, two categories of membership are left for those bodies and organisations joining the ICH after the reform process: Regulatory Members and Industry Members. Regulatory Members can be either legislative and administrative authorities or Regional Harmonisation Initiatives.<sup>97</sup> To acquire membership as a Regulatory Member, a legislative or administrative authority needs to have legal personality and be responsible for the regulation of pharmaceutical products for human use.<sup>98</sup> A Regional Harmonisation Initiative can become a Regulatory Member if it has legal personality and encompasses legislative and/or administrative authorities responsible for the regulation of pharmaceutical products for human use.<sup>99</sup> Furthermore, a Regional Harmonisation Initiative must be able to be represented by either a member authority or a secretariat, while it must also be capable of speaking and committing on behalf of its members.<sup>100</sup> According to the Rules of Procedure of the ICH Assembly, the representation of the RHI should preferably not be carried out by a member of the RHI that is already an ICH member in its own right.<sup>101</sup>

For both Regional Harmonisation Initiatives as well as individual legislative or administrative authorities, a certain legacy of ICH participation is required: in the last two consecutive years before the application, it must have participated in three meetings of the ICH Assembly or three meetings held by the prior form of establishment, the International

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<sup>94</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 10.

<sup>95</sup> See Section 2.2.1.

<sup>96</sup> ICH, Inaugural Assembly of the International Council For Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), 23 October 2015, Final Minutes, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/-Organisational\\_changes/ICH\\_\\_Inaugural\\_Assembly\\_Minutes\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/-Organisational_changes/ICH__Inaugural_Assembly_Minutes_Final.pdf), last accessed: 3 April 2017.

<sup>97</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 11(1) and 11(2).

<sup>98</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11(1).

<sup>99</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11(2).

<sup>100</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11(2).

<sup>101</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 3.

Conference of Harmonisation, immediately before the reform.<sup>102</sup> Additionally, to be eligible for an application the body has to have been appointed experts to two Working Groups of either the Association or the ICH pre-reform, immediately prior to the reform.<sup>103</sup> As a final membership requirement, the Articles of Association foresee the implementation of the ICH Q1, ICH Q7 and ICH E6 Guidelines for individual authorities as well as all members of a Regional Harmonisation Initiative.<sup>104</sup> Thus, in order to become a Regulatory Member, active participation in the ICH process prior to the application, as well as the implementation of a basic set of ICH guidelines, is required.

With regard to Industry Members, eligible for membership application are international organisations, representing the pharmaceutical industry producing products for human use, which have legal personality.<sup>105</sup> Moreover, a certain degree of international character is required, as only organisations with members from ‘several countries in at least three continents’ are eligible.<sup>106</sup> In addition to this requirement, it must be demonstrated that the organisation itself or its members are affected by at least some ICH Guidelines.<sup>107</sup> However, application is only possible where the organisation has been an observer to the Association or was an Interested Party in the pre-reform ICH.<sup>108</sup> Moreover, it needs to have appointed experts in at least two Working Groups either in the Association or the pre-reform ICH immediately before reform.<sup>109</sup>

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<sup>102</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 11(1)(c) and 11(2)(d).

<sup>103</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11(1) (d) and 11(2)(e).

<sup>104</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11(1) and 11(2).

<sup>105</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 12.

<sup>106</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 12(b).

<sup>107</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 12(c).

<sup>108</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 12(d). For former Interested Parties, the Article additionally requires participation in two consecutive years prior to the application in at least 3 Assembly meetings or meetings of the ICH immediately before the reform.

<sup>109</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 12(e).

Aspiring Regulatory Members and Industry Members can submit their application to the ICH Secretariat in writing. Membership is then subject to a decision on admission by the Assembly, which will receive a recommendation from the Management Committee on approval or rejection beforehand.<sup>110</sup> In April 2017, the ICH admitted two Regulatory Members, the Agência Nacional de Vigilância Sanitária (ANVISA, Brazil) and the Ministry of Food and Drug Safety (MFDS, South Korea).<sup>111</sup> The ICH also admitted 3 Industry Members, the International Generic and Biosimilar Medicines Association (IGBA), the World Self-Medication Industry (WSMI), and the Biotechnology Innovation Organisation (BIO).<sup>112</sup>

### 2.2.3 Observers

As well as full membership, it is also possible to obtain observer status within the ICH.<sup>113</sup> The Articles of Association, therefore, now distinguish three different categories of observers:

- Standing Observers,
- Observers, and
- Ad hoc Observers.

The ICH introduced different categories through the reform, according special status to organisations which were observers before, and paying its dues to its own institutional legacy.

The World Health Organisation (WHO) and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) are Standing Observers.<sup>114</sup> While the

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<sup>110</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 13.

<sup>111</sup> <http://www.ich.org/about/membership.html>, last accessed: 3 April 2017.

<sup>112</sup> <http://www.ich.org/about/membership.html>, last accessed: 3 April 2017.

<sup>113</sup> Besides membership, the ICH pre-reform knew of two other categories of participants – observers and interested parties. Observers were non-voting members of the Steering Committee and could also be represented by experts in the working groups. When the Swiss and Canadian regulatory authorities became Steering Committee members, the World Health Organisation (WHO) was the only organisation left with observer status in the ICH, the WHO remained an observer owing to a difference that persisted between the roles of observers between the Swiss and Canadian regulatory authority, and on the WHO. The Swiss and Canadian regulators were committed to not only actively contribute to the process, but also to implement the guidelines that resulted from the harmonization process, whilst the role of the WHO was more geared towards the exchange of information. The WHO informed its members about the ongoing ICH work, and also updated the ICH on current WHO initiatives. In addition to observer status, the ICH also had ‘Interested Parties’, which were organisations that were affected by ICH guidelines. The status of ‘Interested Party’ was granted by the Steering Committee and, upon invitation by the Steering Committee, these parties could nominate members to Working Groups. The World Self-Medication Industry (WSMI) and the International Generic Pharmaceutical Alliance (IGPA) were ‘Interested Parties’ due to the potential effect of ICH guidelines on their work.

<sup>114</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH

WHO always had observer status before the ICH reform, the role of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) was less clearly circumscribed. The IFPMA is the collective organisation of all national/regional research-based pharmaceutical company associations. In the early days of the ICH, the official book compiling the proceedings of the First International Conference on Harmonisation listed the IFPMA as one of the co-sponsors of the Conference<sup>115</sup> and Steering Committee Member,<sup>116</sup> thus placing it on an equal footing with the six other founding parties. However, according to interviews conducted with officials of the Commission and a representative of EFPIA, the role of the IFPMA, apart from hosting the ICH Secretariat, has diminished over time. Today its main role is to keep the national industry associations informed about the ICH process.<sup>117</sup> Thus, before the reform, the IFPMA was not a full member but provided the Secretariat and participated in the Steering Committee without voting rights.<sup>118</sup> According to the IFPMA – together with the WHO – the status of a Standing Observer therefore contributes to clarifying the institutional role of the IFPMA in the ICH.

Besides this category of Standing Observers, the status of ‘Observer’ can be granted to legislative and administrative authorities, supranational bodies and international organisations regulating pharmaceuticals, as well as Regional Harmonisation Initiatives regulating pharmaceuticals, international pharmaceutical industry organisations, and ‘international organisations with an interest in pharmaceuticals’.<sup>119</sup> In all cases, the observer status is granted ‘on the basis of their contribution or benefit to the ICH.’<sup>120</sup> A special provision is introduced for members of the Global Cooperation of the ICH pre-reform, as they were exempted from the application and solely needed to submit a confirmation letter within 3 months of establishment of the Association.<sup>121</sup> In December 2016, observer status had been obtained by nine legislative or administrative authorities, six Regional Harmonisation Initiatives, one International Pharmaceutical Industry Organisation, and four

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Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 16.

<sup>115</sup> P. D’Arcy & D. Harron (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen’s University Belfast, 1992), p. xxii.

<sup>116</sup> D’Arcy & Harron (1992), p. xix.

<sup>117</sup> Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>118</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 4, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/-Process\\_of\\_Harmonisation/ICH\\_Procedures\\_updated\\_July\\_2\\_2015.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/-Process_of_Harmonisation/ICH_Procedures_updated_July_2_2015.pdf), last accessed: 3 April 2017.

<sup>119</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17.

<sup>120</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17.

<sup>121</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17(3).

International Organisations with an Interest in Pharmaceuticals.<sup>122</sup>

Observers will be able to attend the meetings of the ICH Assembly without voting rights.<sup>123</sup> They will, however, not automatically have the right to appoint experts to the Working Groups, but can only do so where this is approved by the Management Committee.<sup>124</sup> A special status is accorded to the Standing Observers, who in addition to the attendance of the Assembly can also attend the Management Committee and will maintain the right to nominate experts for the Working Groups.<sup>125</sup>

Moreover, the Articles of Association introduced the category of Ad-hoc Observers, which are invited by the Assembly or Management Committee to participate in the Assembly meetings.<sup>126</sup> The Rules of Procedure of the Assembly in this regard specify that this category includes ‘entities or bodies... that have not applied for or do not fulfil the criteria for Observership’.<sup>127</sup> The invitations for Ad-hoc Observers to participate in an Assembly meeting will be restricted to specific meetings and the number of Ad-hoc Observers will be kept limited.<sup>128</sup>

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<sup>122</sup> <http://www.ich.org/about/membership.html>, last accessed: 3 April 2017. Legislative and Administrative Authorities: The Central Drugs Standard Control Organization (CDSCO, India), the Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos (CECMED, Cuba), the Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS, Mexico), the Health Sciences Authority (HSA, Singapore), the Medicines Control Council (MCC, South Africa), the National Center for the Expertise of Drugs, Medical Devices and Equipment (National Center, Kazakhstan), the Roszdravnadzor (Russia), the Food and Drug Administration (TFDA, Chinese Taipei) and the Therapeutic Goods Administration (TGA, Australia). Regional Harmonisation Initiatives: The Asia-Pacific Economic Cooperation (APEC), the Association of Southeast Asian Nations (ASEAN), the East African Community (EAC), the Gulf Health Council (GHC), the Pan American Network for Drug Regulatory Harmonization (PANDRH), and the Southern African Development Community (SADC); International Industry Organisations: The Active Pharmaceutical Ingredients Committee (APIC); International Organisations with an Interest in Pharmaceuticals: The Council for International Organizations of Medical Sciences (CIOMS), the European Directorate for the Quality of Medicines & HealthCare (EDQM), the International Pharmaceutical Excipient Council (IPEC) and the United States Pharmacopeia (USP).

<sup>123</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17(4).

<sup>124</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17(5).

<sup>125</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 16.

<sup>126</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 18.

<sup>127</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 9.

<sup>128</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 9.

To conclude, the role of the ICH as a global regulator for pharmaceutical standards has led to the increasing integration of regulators, beyond the three founding regulators. The reform is the final step in this evolution; full membership will be accorded to regulators and Regional Harmonisation Initiatives, which are implementing ICH guidelines, but could not have a voice in the decision-making process until now. In this regard, the institutional structure of the ICH after the reform, according to the interview conducted with Commission officials, will better reflect the de facto global nature of the ICH guidelines.<sup>129</sup> However, the previous assessment also made clear that the institutional structure of the ICH pre-reform, to a certain extent, also carries over to the newly established association, as membership and observership categories differentiate between ‘old’ and ‘new’ actors in the ICH.

### 2.3 *Mandate*

At the inception of the ICH, the founding parties agreed to a mandate of harmonising the technical requirements for the registration of pharmaceutical products throughout the three regions, with regard to the quality, safety and efficacy of a medicinal product, which have to be proven by an applicant wanting to obtain a marketing authorisation. It is important to note, however, that the idea behind the ICH and also its current mandate is not the harmonisation of the marketing authorisation procedure in the sense of a mutual recognition of regulatory assessments in the three regions, nor through a ‘central’ ICH decision that would grant a marketing authorisation for the member markets. Every authority in the ICH regions will continue to carry out their own scientific assessment.

The purpose of the ICH, according to its Articles of Association, is ‘to promote public health through international harmonisation of technical requirements that contributes to the timely introduction of new medicines and continued availability of the approved medicines to patients, to the prevention of unnecessary duplication of clinical trials in humans, to the development, registration and manufacturing of safe, effective, and high quality medicines in an efficient and cost-effective manner, and to the minimisation of the use of animal testing without compromising safety and effectiveness’.<sup>130</sup> The tasks and aims are:

- a) to make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration and the maintenance of such registrations;
- b) to maintain a forum for a constructive dialogue on scientific issues between regulatory authorities and the pharmaceutical industry on the harmonisation of the technical requirements for pharmaceutical products;
- c) to contribute to the protection of public health in the interest of patients from an international perspective;
- d) to monitor and update harmonised technical requirements leading to a greater mutual acceptance of research and development data;

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<sup>129</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>130</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 2.

e) to avoid divergent future requirements through harmonisation of selected topics needed as a result of therapeutic advances and the development of new technologies for the production of medicinal products;

f) to facilitate the adoption of new or improved technical research and development approaches which update or replace current practices;

g) to encourage the implementation and integration of common standards through the dissemination of, the communication of information about and provision of training on, harmonised guidelines and their use; and

h) to develop policy for the ICH Medical Dictionary for Regulatory Activities Terminology (MedDRA) whilst ensuring the scientific and technical maintenance, development and dissemination of MedDRA as a standardised dictionary which facilitates the sharing of regulatory information internationally for medicinal products used by humans.<sup>131</sup>

The ICH thus envisages itself as a platform for exchange ultimately leading to harmonisation, for the benefit of industry and regulators alike, while contributing to public health. Moreover, this mandate stresses the ongoing harmonisation mandate with regard to scientific and technical progress, which can be seen as recognition that the harmonisation of technical requirements is a perpetual exercise, as its scientific basis is in constant change. The public health mandate was only formally taken up in the evolution of the ICH and added to the Terms of Reference in the revision of 2000.<sup>132</sup> However, the first Steering Committee statement provided that ICH ‘activities are pursued in the interest of consumer and public health’.<sup>133</sup>

## 2.4 Funding

An influential trigger for the reform was the funding of the ICH, as prior to the reform the industry parties covered most of the expenses of the ICH. They usually paid the costs for the organisation of the bi-annual meetings, including the travel expenses of some of the participants of the Global Cooperation session. The industry associations covered the costs of the ICH Secretariat.<sup>134</sup> For the European regulators, the Commission compensated the

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<sup>131</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 3. This Article 3 in the Articles of Association largely takes over the ICH ‘Terms of Reference’ which were applicable before the reform: ICH, The Future of ICH – Revised 2000 – Statement by the ICH Steering Committee on the occasion of the Fifth International Conference on Harmonisation, 9-11 November 2000, San Diego, p. 2 (the information has now been removed from the website. A copy is on file with the author).

<sup>132</sup> ICH, The future of ICH – Revised 2000 – Statement by the ICH Steering Committee on the occasion of the Fifth International Conference on Harmonisation, 9-11 November 2000, San Diego, p. 2 (the information has now been removed from the website. A copy is on file with the author).

<sup>133</sup> ICH, Statement by the ICH Steering Committee Tokyo, October 1990, available at: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Vision/ICH\\_SC\\_Statement\\_1990.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Vision/ICH_SC_Statement_1990.pdf), last accessed: 3 April 2017.

<sup>134</sup> European Commission, 70th meeting of the Pharmaceutical Committee, 27 March 2013, PHARM 621, International developments – Agenda Item 5a) Information from the Commission on the Reform of the ICH and the Regulators Forum, p. 2; Interview with an

travel costs of its own staff and the national experts from the EMA Committees participating in the ICH working groups, while the EMA covered the travel costs of its own staff.<sup>135</sup> In a first step towards reforming the reliance on industry funding, the ICH week in November 2014 was paid for by the Commission.<sup>136</sup> However, the industry associations before the reform paid for the large majority of costs for the ICH operation, which led to a dependence of the regulators on industry. In an organisation like the ICH, which has a public health mandate and sets standards that are aimed at protecting patients and ensuring the quality, safety and efficacy of medicinal products, such dependence on the regulated industry is highly problematic.

One of the most important changes that follow from the ICH reform is therefore the new funding structure of the ICH. The aim is to have the attendance of the ICH meetings covered by the respective party itself, while the running costs of the Secretariat and the meetings will be financed through membership fees.<sup>137</sup> Therefore, Article 57 of the Articles of Association foresees that the ICH is to be financed through membership fees to be paid annually, as well as grants or other mechanisms, which the regulatory members can provide in accordance with their law.<sup>138</sup> Moreover, additional means may be generated through participation fees, financial contributions and means generated through the organisation of events and meetings.<sup>139</sup> The membership fee will be determined by the ICH Assembly and may vary for the different categories of members.<sup>140</sup> Until the membership fees are determined, the Founding Regulatory and Industry Members as well as the Standing Regulatory Members will finance the ICH costs for a transitional period.<sup>141</sup>

### 3. THE ICH'S INSTITUTIONAL STRUCTURE

The following section will examine the institutional structure of the ICH and will closely analyse the bodies operating within the ICH, especially with regard to their composition and

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official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>135</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>136</sup> Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>137</sup> ICH, Meeting Report ICH Assembly, Jacksonville, Florida, 9-10 December 2015, p.2, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/B-SC\\_Reports/Assembly\\_report\\_Jacksonville\\_2015.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/B-SC_Reports/Assembly_report_Jacksonville_2015.pdf), last accessed: 3 April 2017.

<sup>138</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 57(2).

<sup>139</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 57(3).

<sup>140</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 58.

<sup>141</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 59.

competence. As the ICH reform is still a very recent development, the section will also briefly summarise the institutional structure of the ICH before the reform.

### 3.1 *The ICH's institutional structure before the reform*

Before the reform, the ICH was composed of a Steering Committee, the Medical Dictionary for Regulatory Activity (MedDRA) Management Board, ICH Working Groups, ICH Coordinators and the ICH Secretariat. Apart from the latter, these bodies were not permanently established. They did not have fixed offices where the members worked on a permanent basis, but were composed of experts of the ICH members meeting on a regular basis in one of the three regions. Thus, the ICH could only be contacted through the Secretariat, which was located at the IFPMA in Geneva.

The institutional structure of the ICH pre-reform was characterised as a two-tier structure, of separating the governance of the harmonisation process as tasks of the Steering Committee, from the process of forming the scientific consensus in the expert working groups. This allowed the ICH to consult very specific expertise in one topic for harmonisation in the working groups, drawing on a network of experts from the respective members. At the same time the Steering Committee, as management and governance body, maintained oversight of the harmonisation process at large and retained the power to finally endorse the guidelines.

The main change brought about by the reform is the abolition of the Steering Committee as main governing body of the ICH, which is replaced by a Management Committee and the Assembly. The Steering Committee (SC) was the focal point of the ICH's work as its main governing body.<sup>142</sup> The Steering Committee decided on the ICH's policies and procedures, thereby determining the ICH's institutional structure and shaping the decision-making process.<sup>143</sup> As well as this general management function, the SC was also responsible for the selection of topics for harmonisation, the appointment of the Working Groups that prepared the guidelines, and scrutinizing the progressing initiatives.<sup>144</sup> In the decision-making process of the guidelines the SC signed off at various stages, confirming the consensus of the ICH members.<sup>145</sup>

Each of the six founding members and later – when Swissmedic and Health Canada became full members, the eight ICH members – had two seats in the Committee, whereas Health Canada only attended with one representative according to the meeting minutes.<sup>146</sup> The EU was usually represented by an official of the European Commission's Directorate General for Health and Food Safety (DG SANTE), and either the Chair of the Vice-Chair of the CHMP.<sup>147</sup> The Steering Committee met every six months.<sup>148</sup>

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<sup>142</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 35.

<sup>143</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 35.

<sup>144</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 35.

<sup>145</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 36.

<sup>146</sup> See: ICH, Meeting Report ICH Assembly, Jacksonville, Florida, 9-10 December 2015, p. 2.

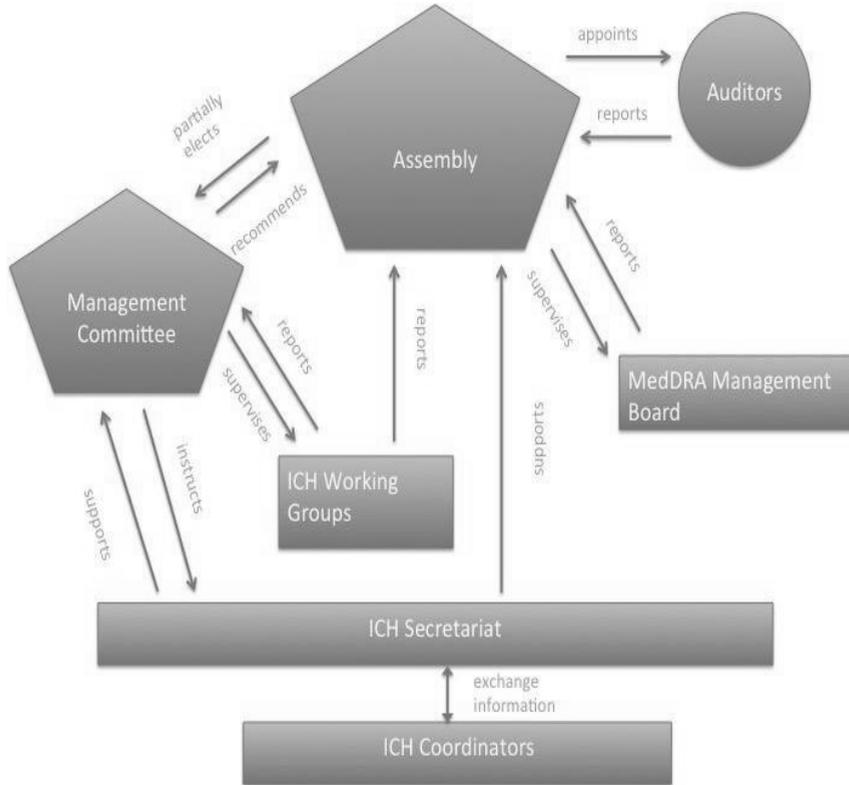
<sup>147</sup> Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>148</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 35.

### 3.2 The ICH's institutional structure after the reform

After the reform, Article 20 of the Articles of Association lists the bodies of the Association as the Assembly, the Management Committee, the MedDRA Management Committee, the ICH Secretariat and the Auditors.<sup>149</sup>

**Figure 1: ICH institutional structure post-reform**



As indicated, the Management Committee and the Assembly of ICH Members, which now form the main decision-making bodies of the ICH, have replaced the Steering Committee through the reform. Where the Assembly is the central decision-making body in the ICH, the Management Committee is responsible for administrative and managerial tasks. This dual governing-body structure is in accordance with the Swiss Civil Code.<sup>150</sup>

However, the two-tier structure of separating the management, governance and decision-making in the Management Committee and the Assembly from the forming of

<sup>149</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 20.

<sup>150</sup> Swiss Civil Code of 10 December 1907, Status as of 1 January 2017, Arts. 65 jo 69.

scientific consensus on specific guidelines in Expert Working Groups is maintained. The Expert Working Groups do not form bodies of the Association according to the Articles of Association, which might be due to the fact that they are created and abolished in accordance with the execution of a specific task, such as the drafting of a new ICH guideline. As they form an important part of the ICH institutional structure nonetheless, they will be discussed in this section as well. Moreover, although not mentioned in Article 20 of the Articles of Association, the ICH Coordinators are an important part of the institutional structure of the ICH, so they will be discussed as well. This section will first discuss the ICH bodies as enlisted in Article 20 and proceed to analysing the Working Groups and the ICH Coordinators.

### 3.2.1 The Assembly

Articles 21 to 26 of the ICH Articles of Association regulate the Assembly, which consists of all ICH members,<sup>151</sup> which are each entitled to participate in the meetings with two representatives.<sup>152</sup> Moreover, the Standing Observers and Observers attend the Assembly with two representatives, however, without voting rights.<sup>153</sup> The Standing Observers and Observers can actively participate in this discussion and voice their opinion on respective matters.<sup>154</sup>

The Assembly meets annually as a minimum. Additional meetings and extraordinarily meetings at shorter notice can take place if the Management Committee decides accordingly.<sup>155</sup> According to the Rules of Procedure of the Assembly, two meetings per year in spring and autumn have been agreed, as was the case prior to the reform.<sup>156</sup> The Management Committee will determine when and where the Assembly will take place as well as its duration.<sup>157</sup> Moreover, with the assistance of the ICH Secretariat and taking the agenda items proposed by members into account the Management Committee also prepares the

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<sup>151</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 21.

<sup>152</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 24.

<sup>153</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 16 and 17.

<sup>154</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 14.

<sup>155</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 23(1) and (5).

<sup>156</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 11.

<sup>157</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 23(2).

agenda.<sup>158</sup>

According to the Articles of Association, the Assembly forms ‘the overarching body of the Association’.<sup>159</sup> It has competence to adopt and amend the Articles of Association as well as its own Rules of Procedure, and is able to dissolve the Association.<sup>160</sup> Importantly for this research, the Assembly is assigned the task of approving new topics for harmonisation in the form of ICH guidelines, and has competence to adopt, amend and withdraw guidelines.<sup>161</sup> Furthermore, it has the task of appointing elected members to the Management Committee and has the competence to dismiss both Elected and Permanent Management Committee Representatives.<sup>162</sup> It also approves the work plan and annual report of the MedDRA and approves the MedDRA budget.<sup>163</sup>

Moreover, the Assembly is the main decision-making body with regard to the admission or refusal of applications for ICH membership and observership, and also of their exclusion.<sup>164</sup> It also determines the membership fees.<sup>165</sup> The Assembly appoints and dismisses the Auditors, approves the annual accounts after they have been audited, and also approves the ICH’s budget for the coming fiscal year.<sup>166</sup> The Assembly has important control functions, as it approves the annual report of ICH activities drafted by the

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<sup>158</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 23 (3) and (4).

<sup>159</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22.

<sup>160</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 22(1)(a), (b) and (l).

<sup>161</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(r).

<sup>162</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 22(1)(g) and (h).

<sup>163</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(q).

<sup>164</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(c)-(f).

<sup>165</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(m).

<sup>166</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(i), (o) and (p).

Management Committee and will discharge the activities of the other bodies of the Association.<sup>167</sup> In addition to that, it approves the annual work plan as well as the multi-annual strategic plan, and is responsible for approving cooperation with other organisations.<sup>168</sup>

It elects a Chair and Vice-Chair for a period of two years with possible re-election, who can be accompanied by an associate Vice-Chair to be appointed by the Member hosting the Assembly for that meeting.<sup>169</sup> The Chair can only be elected amongst the Founding Regulatory Members, the Standing Regulatory Members or the Regulatory Members of the Management Committee, whereas the Vice-Chair can be elected amongst the Founding Regulatory Members, the Standing Regulatory Members or the Regulatory Members of the Assembly.<sup>170</sup> Thus, in any case, the Chair and Vice-Chair will be representatives of a regulatory member and will not be industry representatives.

In the Assembly, consensus will be the core decision-making principle.<sup>171</sup> A written procedure can be used if the Assembly decision is consensual.<sup>172</sup> Only where the Assembly fails to reach a decision by consensus will it vote on the decision.<sup>173</sup> In order to establish a quorum, all Founding Regulatory Members, one Founding Industry Member and one Standing Regulatory Member have to be present.<sup>174</sup> According to the Rules of Procedure of the Assembly, the Chair can agree to several rounds of discussion and may also postpone a

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<sup>167</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(j) and (k).

<sup>168</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22(1)(n) and (s).

<sup>169</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 23(6).

<sup>170</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 23(6).

<sup>171</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(2).

<sup>172</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(8).

<sup>173</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(2).

<sup>174</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(1).

decision by vote.<sup>175</sup> Where a decision is taken by vote, each member will be assigned one vote.<sup>176</sup> The required majority will differ with regard to the types of decision: for example, a three-quarter majority, which must include the votes of each Founding Regulatory Members, is necessary to amend the Articles of Association.<sup>177</sup> The voting on the selection of harmonisation topics, as well as adoption, amendment and withdrawal of ICH guidelines, will be discussed in detail in the section on the guidelines adoption procedure later in this research.<sup>178</sup> The Assembly generally takes its decision by open ballot, apart from the votes on the Elected Management Committee Representatives and the election of the Chair and Vice-Chair of the Assembly.<sup>179</sup> However, the Chair may opt for a secret ballot in other cases upon request of one Member, if this request is supported by at least one other Member.<sup>180</sup>

### 3.2.2 Management Committee

The Management Committee has been entrusted with the ‘operational aspects’ and specifically the ‘administrative and financial matters’ of the ICH.<sup>181</sup> It operates under the Articles of Association and its Rules of Procedure.<sup>182</sup> The Management Committee has a total of 28 members, whereas 16 are Permanent Management Committee Representatives and 12 are Elected Management Committee Representatives.<sup>183</sup> For a transitional period,

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<sup>175</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 14.

<sup>176</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(2).

<sup>177</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(3).

<sup>178</sup> Section 4.1.

<sup>179</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(9).

<sup>180</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(9).

<sup>181</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(1).

<sup>182</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Management Committee, Approved by the Management Committee on 8 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_MC\\_RoPs\\_Approved\\_by\\_Assembly\\_final\\_8Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_MC_RoPs_Approved_by_Assembly_final_8Nov2016.pdf), last accessed: 3 April 2017.

<sup>183</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 27(3).

until the reform is fully employed or until 1 January 2018, an inaugural Management Committee with 16 Permanent Management Committee Representatives has been established.<sup>184</sup> Alongside the members, the WHO and IFPMA will attend the Management Committee as Permanent Observers with two delegates each.<sup>185</sup>

It is the role of the Permanent Management Committee Representatives to represent the Founding Regulatory Members, Founding Industry Members and Standing Regulatory Members. This essentially covers all of the members who were parties to the ICH pre-reform – EU, US and Japanese regulators, industry representatives, as well as Health Canada and Swissmedic. They are entitled to two Permanent Management Committee Representatives per member.<sup>186</sup> These Permanent Management Committee Representatives have an indefinite term of office.<sup>187</sup>

Furthermore, the Assembly will elect the Elected Management Committee Representatives for a term of office of four years, with a possibility of reelection.<sup>188</sup> There will be up to eight Elected Management Committee Representatives, which represent four Regulatory Members with two representatives each.<sup>189</sup> Moreover, the Industry Members are entitled to four Elected Management Representatives representing two Industry Members.<sup>190</sup> Regulatory Members are eligible to propose representatives, as long as they have actively participated in all ICH meetings for the last four consecutive years, provided experts in at least two Working Groups, and have a good implementation record concerning ICH guidelines.<sup>191</sup> Industry Members can propose representatives for the Management

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<sup>184</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 27(2) and (3).

<sup>185</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 27(4).

<sup>186</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 28.

<sup>187</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 27(2).

<sup>188</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 27(3).

<sup>189</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 27(3).

<sup>190</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 27(3).

<sup>191</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 29(1).

Committee where they have participated in all Assembly meetings in the four years prior to the election, had experts participating in Working Groups in the four years prior to the election, and can demonstrate that they or their members are affected by most of the ICH guidelines.<sup>192</sup>

The Management Board meets whenever necessary, but at least whenever the Assembly is meeting, either face to face, by phone or through video conferences.<sup>193</sup> In these meetings a Management Committee Representative representing a Permanent Regulatory Member chairs the Management Committee. The respective member will, for the duration of the chairing term, be eligible to appoint another Management Committee Representative.<sup>194</sup>

All Management Committee Representatives are expected to act in the interest of the member they represent. However, the members are also asked to act in the interest of the Association.<sup>195</sup> In this respect, the Management Committee has extensive competences in the management and administration of the ICH. It decides which member will host the Assembly meetings and prepare as well as convene those meetings.<sup>196</sup> Moreover, the Management Committee submits recommendations and proposals for Assembly decision, including the annual work plan and multi-annual strategic plan, recommendations for harmonisation topics and proposals on the adoption, amendment or withdrawal of ICH guidelines, as well as recommendations regarding the membership and observership applications.<sup>197</sup> Thus, although the Assembly is the main decision-making body of the ICH, the Management Committee has a strong influence on the decisions taken. The Management Committee appoints and dismisses the Director heading the ICH Secretariat and regulates his competences and responsibilities.<sup>198</sup> Furthermore, it designates persons to represent the

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<sup>192</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 30(1).

<sup>193</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 36(1).

<sup>194</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 36(2).

<sup>195</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 34(2).

<sup>196</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 35(2)(a) and (b).

<sup>197</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(c), (g) and (h).

<sup>198</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(d).

ICH externally.<sup>199</sup>

The Management Committee is also responsible for supervising the Working Groups, with regard to an efficient harmonisation process and high quality guidelines.<sup>200</sup> Additionally, the Management Committee has certain financial competences as it will determine the membership fees, while the reform is still ongoing, and later proposes membership fees to the Assembly.<sup>201</sup> It submits the audited annual accounts to the Assembly, makes proposals and recommendations on financial matters, such as the draft budget, to be decided on by the Assembly, and deals with liability questions such as insurance.<sup>202</sup>

To fulfil all of these duties, the Management Committee can establish sub-committees and working groups in accordance with its Rules of Procedure.<sup>203</sup> The Management Committee has the competence to supervise these sub-committees, deciding on their program and approving their reports.<sup>204</sup>

The main decision-making principle in the Management Committee is consensus, however, qualified majority voting will be adhered to where reaching consensus on a decision fails.<sup>205</sup> The votes will be cast per member, which means that the two representatives per member will have one vote to exercise jointly.<sup>206</sup> The precise voting requirements differ with regard to the type of decision that has to be taken. Where a decision on administrative and organisational matters which does not have financial consequences is taken, a two-thirds majority is required. This two-thirds majority must encompass the votes

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<sup>199</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(e).

<sup>200</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(f).

<sup>201</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(j).

<sup>202</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(k), (l) and (m).

<sup>203</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(3).

<sup>204</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(i).

<sup>205</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(4).

<sup>206</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Art. 37(3).

of the representatives of all three Founding Regulatory Members.<sup>207</sup> If the Management Committee fails to reach a two-thirds majority, the decision-making will proceed with only the Permanent Management Committee Representatives of the Founding Regulatory Members having a voice and a unanimity requirement amongst these representatives.<sup>208</sup> The same procedure is also applicable for decisions on the selection of topics for guidelines and adoption, amendment or withdrawal of ICH guidelines,<sup>209</sup> as the Management Committee makes recommendations and proposals on this to the Assembly.<sup>210</sup> Where the Management Committee decides on financial matters, a two-thirds majority including the votes of the representatives of the Founding Regulatory Members is also required.<sup>211</sup> However, where obtaining the two-thirds majority fails, the procedure does not foresee that unanimity between the Founding Regulatory Members could replace the two-thirds majority.<sup>212</sup>

### 3.2.3 MedDRA Management Board

The Medical Dictionary for Regulatory Activity (MedDRA) produced and managed by the ICH lays down the standard medical terminology for international use, which is applicable through all stages of a medicinal product, from development to the monitoring of products on the market.<sup>213</sup> Thus, whereas the ICH guidelines lay down scientific requirements like testing procedures, the MedDRA harmonises the terminology used by regulators and industry in these guidance documents, applications and in other communication.

The task of the MedDRA Management Board, which is a body of the Association,<sup>214</sup> is the coordination and control of MedDRA activities, including the supervision of the Maintenance and Support Services Organisation (MSSO), to which the MedDRA

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<sup>207</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(5).

<sup>208</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(5).

<sup>209</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(7).

<sup>210</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(g).

<sup>211</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(6).

<sup>212</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(6).

<sup>213</sup> <http://www.meddra.org/about-meddra/vision>, last accessed: 3 April 2017.

<sup>214</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 20.

Management Board can outsource the day-to-day work regarding the maintenance and advancement of the medical dictionary.<sup>215</sup> In its activities the MedDRA Management Board is supported by the MedDRA Secretariat, which closely cooperates with the ICH Secretariat.<sup>216</sup>

The MedDRA Management Board is composed of up to two representatives of each Founding Regulatory Members, Founding Industry Members and Standing Regulatory Members, as well as two representatives of the Medicines and Healthcare products Agency of the UK.<sup>217</sup> Moreover, the WHO may participate in the meetings with two delegates as observers.<sup>218</sup>

### 3.2.4 ICH Secretariat

Before the ICH reform, the Secretariat of the ICH was hosted by the IFPMA in Geneva. According to information provided by Commission officials in an interview conducted for this research, although the Secretariat was hosted by the IFPMA, they were separate from the IFPMA as such.<sup>219</sup> The IFPMA provided the offices and contracts, but the Secretariat was separated from the IFPMA matters and was instructed by the ICH Steering Committee.<sup>220</sup> However, as the ICH Secretariat has an important function in coordinating the ICH process, it deserved critical attention that the Secretariat was hosted by the IFPMA, the global industry representation, and was not an independent body.

With the reform, the institutional role of the ICH Secretariat has changed and it is now a body of the Association.<sup>221</sup> Under the new Articles of Association the ICH provides the salaries for the Secretariat and its Director.<sup>222</sup> However, at the time of writing, the contact address of the ICH Secretariat is still the same as the IFPMA office, and it is unclear whether

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<sup>215</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 46(1).

<sup>216</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 51.

<sup>217</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 42 and 43.

<sup>218</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 42(3).

<sup>219</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>220</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>221</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 20.

<sup>222</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 53.

physical relocation is actually planned.<sup>223</sup>

A Director, who is supervised by the Management Committee, heads the Secretariat.<sup>224</sup> The responsibilities assigned to the Secretariat are the daily management of the ICH,<sup>225</sup> including assistance to the Management Committee in the preparation of the budgets and supporting any sub-committees or working groups, as well as the coordination of ICH activities.<sup>226</sup> Moreover, the Secretariat will represent the ICH externally, whereas the Management Committee will decide on the power of signature.<sup>227</sup> In addition to that, the Secretariat staff attends ICH Assembly meetings and supports the Chair and Vice-Chair.<sup>228</sup> Further detail on the task and organisation of the ICH Secretariat will be laid down in an Employee Handbook, which was not publicly available at the time of writing.<sup>229</sup>

In the interviews conducted for this research, officials of the Commission, EMA and the representative of EFPIA underlined the importance of the coordinative role of the ICH Secretariat for the harmonisation process.<sup>230</sup> Those working at the Secretariat are highly qualified and often have a medical background, meaning that they comprehend the harmonisation process, also with regard to the scientific content.<sup>231</sup> However, their role in ensuring that the harmonisation process moves forward, and preparing the meetings is key to facilitating the progress in harmonisation where the members are active in so many organisational entities.

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<sup>223</sup> <http://www.ich.org/about/organisation-of-ich/secretariat.html>, last accessed: 3 April 2017; <http://www.ifpma.org>, last accessed: 3 April 2017.

<sup>224</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 53.

<sup>225</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 54(1).

<sup>226</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 54(2).

<sup>227</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 54(1).

<sup>228</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 14.

<sup>229</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 54(3).

<sup>230</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author; Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>231</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

### 3.2.5 Auditors

Listed in Article 20 of the Articles of Association as an official body of the ICH, the Auditors are assigned the annual audit of the financial statements of the ICH under Swiss law and accounting principles.<sup>232</sup> This task is assigned to an auditing firm subject to appointment by the Assembly for a period of two years with the possibility of dismissal at any time.<sup>233</sup> A written report of the annual audit is provided to the Assembly.<sup>234</sup>

### 3.2.6 Working Groups

The Working Groups do not appear as bodies of the ICH in the Articles of Association. Their working process is clarified in the Standard Operating Procedure (SOP) of the ICH Working Groups.<sup>235</sup>

These Working Groups take the form of an:

- Expert Working Group (EWG);
- Implementation Working Group (IWG); or
- Informal Working Group.

The Expert Working Groups (EWGs) are established to draft a new ICH guideline and coordinate scientific and technical aspects of a specific harmonisation topic, working towards scientific consensus in the matter.<sup>236</sup> Alongside the EWGs, Implementation Working Groups (IWGs) develop Q&A documents, which are meant to assist the implementation of the Guidelines.<sup>237</sup> The Informal Working Groups are established before the formal start of harmonisation activities and develop the Concept Paper and Business Plan for an upcoming harmonisation topic.<sup>238</sup> The ICH also knows Discussion Groups,

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<sup>232</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 56.

<sup>233</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 55.

<sup>234</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 56.

<sup>235</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/-Articles\\_Procedures/ICH\\_EWG\\_IWG\\_SOP\\_final\\_1Dec2016\\_Osaka\\_v2.0.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/-Articles_Procedures/ICH_EWG_IWG_SOP_final_1Dec2016_Osaka_v2.0.pdf), last accessed: 3 April 2017.

<sup>236</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. v.

<sup>237</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. vi.

<sup>238</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0,

which are formed to debate certain scientific consideration documents. These documents are not adopted following the formal ICH procedure, but are only endorsed by the Steering Committee. Discussion Groups have worked on the gene therapy as well as the participation of women in clinical trials.<sup>239</sup>

An Informal Working Group is established whenever the Assembly decides to approve a new topic for an ICH guideline, while an Expert Working Group will be established, after approval of the Concept and Business Paper developed by the Informal Working Group.<sup>240</sup>

The Working Groups do not have a fixed meeting rhythm, since they carry out most of their work through writing and teleconferences. They only meet in person where this is necessary.<sup>241</sup> With regard to the Expert Working Groups the Standard Operating procedure provides that while face-to-face meetings – if they are scheduled – usually take place in conjunction with Assembly meetings, not every Expert Working Group will meet face-to-face each time the Assembly meets, but only if a meeting is necessary and approved by the Management Committee.<sup>242</sup>

The membership of the EWGs and IWGs fluctuates. For every topic, a new group with new experts is established. Each member will be allowed to appoint up to two experts for each Working Group,<sup>243</sup> whereas the Founding Regulatory Members are required to appoint experts.<sup>244</sup> In exceptional cases, the cap of two experts per Working Group may be lifted for the Founding Regulatory Members and Founding Industry Members, where this is necessary, in order to have sufficient expertise in the group.<sup>245</sup> Standing Observers and Observers are also allowed to nominate one expert for participation in a Working Group.<sup>246</sup> An observer's participation is subject to approval of the Management

Last update by the ICH Management Committee on 8 November 2016, p. vi. See further: Section 4.1.

<sup>239</sup> <http://www.ich.org/products/consideration-documents.html>, last accessed: 3 April 2017.

<sup>240</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 4 and 9. See further: Section 4.1.

<sup>241</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 15.

<sup>242</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 15.

<sup>243</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2017, p. 17; ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 9.

<sup>244</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 9.

<sup>245</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 9.

<sup>246</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 9.

Committee.<sup>247</sup> However, the Management Committee may limit the nomination of experts by Regulatory Members and Industry Members, where the size of the group becomes excessive and ineffective.<sup>248</sup> In general, Working Groups should not have more than 25 to 30 members.<sup>249</sup>

The experts appointed are expected to have the necessary expertise in the topic the Working Group is concerned with, and they should actively and continuously participate in the discussions.<sup>250</sup> Moreover, it is established that in order to have a quorum, at least one representative of each Founding Regulatory Member is required to be present and, where Founding Industry Members and/or Standing Regulatory Members have appointed experts, at least one expert of the respective parties should also be present.<sup>251</sup> For the EU, the members are usually appointed from the experts of the CHMP or the CHMP working groups, and are occasionally also nominated from EMA staff.<sup>252</sup> The positions taken by these experts at the ICH working group level are reconfirmed within the scientific EMA committees and their working groups, who will discuss the topics at an EU level as the discussion progresses at the global level.<sup>253</sup>

Within each group, a Regulatory Chair is appointed by the Regulatory Members of the Management Committee, to represent the Regulatory Members.<sup>254</sup> The Regulatory Chair will ensure that the consensus-building process is streamlined according to the scope of the harmonisation, and will be executed according to the agreed upon deadlines.<sup>255</sup> A Rapporteur will be appointed by the Assembly amongst the representatives of any members; however, if the Rapporteur is an industry representative, a regulatory representative will

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<sup>247</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17(5).

<sup>248</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 19.

<sup>249</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 19.

<sup>250</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 9.

<sup>251</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 23.

<sup>252</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>253</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author; Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>254</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 9ff.

<sup>255</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 10ff.

replace this Rapporteur in Step 2b of the decision-making process.<sup>256</sup> The Rapporteur is appointed to coordinate the scientific work of the group and draft the documents.<sup>257</sup> Where the Rapporteur is appointed, the respective member is allowed to appoint an additional expert to the Working Group.<sup>258</sup>

### 3.2.7 ICH Coordinators

Each of the members should appoint an ICH Coordinator to function as a contact point within the respective member's organisation for the ICH Secretariat.<sup>259</sup> They are specifically responsible for the facilitation of information exchange between the experts of the members and the ICH Secretariat, safeguarding ICH documents to reach the appropriate persons and to support the Working Groups.<sup>260</sup> Members may also designate an ICH Technical Coordinator, with the task of supporting their respective Assembly and/or Management Committee representative with their scientific knowledge.<sup>261</sup> Before the ICH reform these Coordinators were presented as an integral part of the ICH institutional structure and the harmonisation process.<sup>262</sup> After the reform, the ICH Articles of Association do not mention the ICH Coordinators and they are not bodies of the Association, however, the Rules of Procedure of the Assembly show that they also exist after the reform.<sup>263</sup> However, the Standard Operating Procedure for Working Groups clarifies that ICH Coordinators 'play a fundamental role in the efficient operations of the ICH Association'.<sup>264</sup>

## 4. ICH STANDARD-SETTING PROCESS

The ICH has pronounced the promotion of 'public health through international harmonisation of technical requirements'<sup>265</sup> as its purpose, which they carry out through the

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<sup>256</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 13.

<sup>257</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 14.

<sup>258</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 12.

<sup>259</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 8.

<sup>260</sup> A detailed list of tasks of the ICH Coordinators is provided in the Standard Operating Procedure for ICH Working Groups. See: ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 32ff.

<sup>261</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 34.

<sup>262</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 36.

<sup>263</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 15 June 2016, p. 7.

<sup>264</sup> ICH, Standard Operating Procedures for the ICH Working Groups, p. 29.

<sup>265</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH

adoption of ICH guidelines. This section examines the procedure for creating these guidelines and discusses the effect of the recent ICH reform on the influence of the industry representative within the standard-setting process.

Before entering into the analysis of ICH standards, it should be mentioned that the ICH has four different procedures:

- the Formal ICH Procedure, which is used to establish new guidelines;
- the Q&A Procedure, which is applicable to the drafting of Q&A documents to provide further information on a guideline, in order to ensure the correct implementation of ICH guidelines;
- the Revision Procedure, which serves the adaptation of guidelines, either through amendments or through an addendum or an annex; and
- the Maintenance Procedure, used to update an existing guideline.<sup>266</sup>

As the focus of this research is on regulatory standards, the Formal ICH procedure used for the adoption of the ICH guidelines is the relevant procedure that needs to be analysed closely.

#### 4.1 *Formal ICH Procedure: standard-setting in five steps*

Standard-setting in the ICH occurs through the Formal ICH Procedure in a five-step pattern. However, before the actual five step standard-setting process begins, a topic for harmonisation has to be selected. The selection of a new topic for harmonisation in the form of an ICH guideline starts with a party or an observer proposing a topic to the Management Committee, through filling out the New Topic Proposal Template.<sup>267</sup> The decision on whether a topic is adopted for harmonisation is taken by the Assembly, which receives a recommendation on new topics from the Management Committee.<sup>268</sup> This means that the choice of a new harmonisation topic is subject to two decision-making stages: a decision on a recommendation by the Management Committee, and a decision on the adoption of a topic for harmonisation by the Assembly, both of which are subject to separate decision-making rules.

First of all, the Management Committee will adopt a recommendation on the selection of a new topic. The Management Committee adheres to consensus decision-making and only shifts to voting where consensus cannot be obtained.<sup>269</sup> Where the Management Committee

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Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 2.

<sup>266</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 1.

<sup>267</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 4.

<sup>268</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 22 (1)(r) jo. Art. 35(2)(g).

<sup>269</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(4).

cannot reach consensus on a recommendation regarding a proposed harmonisation topic, a qualified majority voting according to Article 37(7) of the Articles of Association should take place. Then, a two-thirds majority of votes cast is necessary to adopt a decision, and the two-thirds majority must include the votes by the representatives of the Founding Regulatory Members.<sup>270</sup> As Article 37(3) only excludes the representatives of the Founding Industry Members and the Industry Members from voting on the adoption, amendment and withdrawal of ICH guidelines in the Management Committee, at this initial phase of choosing a topic for harmonisation, they are able to vote and form part of the two-thirds majority requirement.<sup>271</sup> Where a two-thirds majority is not obtainable, the decision will be taken by unanimity of the representatives of the Founding Regulatory Members.<sup>272</sup> The recommendation of the Management Committee on a new harmonisation topic is then submitted to the Assembly.

In a second stage, the decision of the Assembly on a topic proposed for harmonisation is in principle taken by consensus,<sup>273</sup> which means that all members take part in the discussions regarding proposed topics for harmonisation, and can express their opinions on the matter.<sup>274</sup> However, where consensus cannot be achieved and the Assembly has to take a vote on the proposal, the Founding Industry Members and the Industry Members are excluded from voting.<sup>275</sup> Before the actual voting takes place, the members that represent regulators will be asked to present their views, and the Chair will take a decision whether consensus will be achievable or whether the Assembly shall proceed with voting on a topic.<sup>276</sup> In this case, a simple majority of the votes exercised by the Founding Regulatory Members, Standing Regulatory Members and Regulatory Members, which needs to include the votes of all Founding Regulatory Members, will be decisive for the adoption of a new

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<sup>270</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(7).

<sup>271</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(3).

<sup>272</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(7).

<sup>273</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(2).

<sup>274</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 15.

<sup>275</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(2) jo. Art. 9(2)(a) and Art. 12(2)(b).

<sup>276</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 15.

topic for harmonisation.<sup>277</sup>

The decision-making procedure in the Assembly means that industry members will not be able to influence the choice of a topic for harmonisation, where a consensus cannot be reached and a vote has to take place. The fact that the regulators will ultimately decide on the harmonisation topic is justified in the Rules of Procedure of the Assembly, by stating that ‘regulators have the ultimate responsibility to ensure the protection of public health and have the responsibility to issue regulatory guidelines’.<sup>278</sup> Nonetheless, the Articles of Association oblige the members with voting rights on the selection of new harmonisation topics to ‘in good faith, consider the opinions expressed by other Members’.<sup>279</sup>

Where a proposed topic is chosen for harmonisation an informal Working Group is established to develop a Concept Paper, which entails a statement of the perceived problem, and outlines the issues that a harmonisation should resolve.<sup>280</sup> Moreover a Business Plan, providing an overview of the costs and benefits of adopting a topic for harmonisation, is developed in the informal Working Group for a new topic.<sup>281</sup> The informal Working Group will be composed of at least one expert of every Founding Member, while other members can nominate up to two experts and observers can nominate one expert.<sup>282</sup> The informal Working Groups should not have more than 25 to 30 members, and the member proposing a topic for harmonisation will be offered the opportunity to nominate the expert leading the group.<sup>283</sup> The Concept Paper and Business Plan are subject to endorsement by the Management Committee.<sup>284</sup>

When the Concept Paper and Business Plan are approved, an Expert Working Group is established. The members that want to appoint experts to the Working Groups submit names to the ICH Secretariat.<sup>285</sup> Then a Regulatory Chair and a Rapporteur are appointed

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<sup>277</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(5).

<sup>278</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>279</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(5).

<sup>280</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. v.

<sup>281</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. v.

<sup>282</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 6.

<sup>283</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 6.

<sup>284</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 7 and 8.

<sup>285</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10

for each Expert Working Group. Expressions of interest of the eligible parties can be submitted to the Secretariat as soon as a new topic for harmonisation is on the Agenda of the Assembly, and upon request of the Chair during the Assembly.<sup>286</sup> When the Expert Working Group is set up and the Regulatory Chair as well as the Rapporteur are appointed, the actual five-step procedure starts.

**Figure 2: ICH standard-setting process**



In Step 1 scientific consensus on the harmonisation topic is formed. The Expert Working Group works towards a consensus in the form of a ‘Technical Document’ for the respective topic assigned to them.<sup>287</sup> Within the Expert Working Groups, each member will be responsible for ensuring that the internal rules of this member are adhered to.<sup>288</sup> A Rapporteur will draft the technical document based on the consultations carried out with the experts in the Working Group.<sup>289</sup> This process usually takes place via a written procedure or

December 2015, Last update approved by the Assembly on 16 November 2016, p. 19. Regarding the eligibility to appoint expert to the working groups see Section 3.2.6.

<sup>286</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 19. Regarding the eligibility to become Regulatory Chair and Rapporteur see Section 3.2.6.

<sup>287</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 17.

<sup>288</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 17.

<sup>289</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 17.

teleconferences as the EWGs only meet during the ICH week, which means that the meetings now take place in parallel to the Assembly and Management Committee meetings.<sup>290</sup> The Management Committee under Article 35(2)(f) of the Articles of Association has the task of overseeing the Working Group process.<sup>291</sup> The Expert Working Groups, in this regard, will regularly provide work plans to the Management Committee. The Expert Working Group Chair or the Rapporteur may have to provide additional reports either in written or oral form to the Management Committee.<sup>292</sup> However, according to the Rules of Procedure of the Assembly, the Regulatory Chair and/or the Rapporteur, together with the respective experts of the Working Groups gathering during the ICH meeting, will also be invited to attend the Assembly for this agenda item, to report about the harmonisation process.<sup>293</sup> Where an agreement on the topic is reached in the Working Group, the members of the EWG sign a ‘Step 1 Experts Sign-off sheet’ and set up the ‘Step 1 Technical Document’ which is submitted to the Assembly.<sup>294</sup>

In *Step 2*, the scientific consensus expressed in the Technical Document is confirmed by the Assembly.<sup>295</sup> In *Step 2a* the members of the Assembly have to be in agreement that there is scientific consensus and, at this stage, the views of all members including the members representing industry are taken into account for the consensus.<sup>296</sup> However, ‘(i)n the unlikely situation where consensus cannot be reached, the Assembly will proceed to voting’ in order to adopt the Final Technical Document by majority.<sup>297</sup> This Final Technical Document then will be developed into a Draft Guideline. Whereas the industry experts in the respective Working Group are fully part of the development of the Technical Document until *Step 2a*,<sup>298</sup> the development of the Draft Guideline in *Step 2b* is regulator-driven. However according to the Rules of Procedure of the Assembly, the experts nominated by

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<sup>290</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 18.

<sup>291</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 35(2)(f).

<sup>292</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Management Committee, Approved by the Management Committee on 16 June 2016, Last update approved by the Management Committee on 8 November 2016, p. 12f.

<sup>293</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>294</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 18.

<sup>295</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>296</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>297</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 19.

<sup>298</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 20f.

the Founding Industry Members and Industry Members remain members of the Working Group and participate in the process.<sup>299</sup> *Step 2b* is concluded by the endorsement of the Draft Guideline through the Assembly, for which only the views of the members representing regulators are taken into account for the consensus.<sup>300</sup> Again, where consensus fails, the Regulatory Members of the Assembly can adopt the Draft Guideline by majority vote.<sup>301</sup> After *Step 2*, the Draft Guideline will be published on the ICH website.<sup>302</sup>

*Step 3* is characterised by a public consultation procedure. The Draft Guideline is submitted to the regulatory authorities of the ICH Members for public consultation according to their national procedures.<sup>303</sup> Comments on the Draft Guideline can be submitted to the regulatory authorities according to the usual national procedure. According to the Standard Operating Procedure for Working Groups, this consultation may take from anywhere between 30 days up to six months.<sup>304</sup> In the EU, it will be published as a draft CHMP Guideline, the CHMP being the Committee for Human Medicinal Products within the European Medicines Agency (EMA).<sup>305</sup> In addition, the draft is published by the ICH Secretariat for comments.<sup>306</sup> The Regulatory Members will review the received comments.<sup>307</sup> The comments are then forwarded to the EWG, which will consider the comments and on this basis write a revised version of the Draft Guidelines, which is called '*Step 3 Expert Draft Guideline*'.<sup>308</sup> After the consultation procedure, if the responsible rapporteur is the

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<sup>299</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 20f.

<sup>300</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>301</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>302</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21.

<sup>303</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21.

<sup>304</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21.

<sup>305</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21. The role of the EMA in the implementation of the ICH guidelines will be discussed in Chapter 5. A closer examination of the public consultation procedure is provided in Chapter 6, Section 2.

<sup>306</sup> <http://www.ich.org/products/open-consultation.html>, last accessed: 3 April 2017.

<sup>307</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21.

<sup>308</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working

representative of the industry, a new one is appointed from the representatives of the regulatory bodies.<sup>309</sup> The final draft is then signed by the EWG representatives from the regulatory authorities and sent to the Assembly.<sup>310</sup>

At *Step 4*, the adoption of the ICH Guideline follows. Like the adoption of a new topic for harmonisation, the adoption of a finalised guideline is also subject to two decision-making stages: a decision on a recommendation by the Management Committee, and a decision on the adoption of the guideline by the Assembly.

Firstly, the Management Committee will adopt a recommendation on the adoption of a guideline. Again, the core decision-making principle is consensus.<sup>311</sup> Where the Management Committee, cannot reach consensus, a qualified majority voting according to Article 37(7) of the Articles of Association should take place. A two-thirds majority of votes cast is necessary to adopt a decision, whereas the two-thirds majority must include the votes by the representatives of the Founding Regulatory Members.<sup>312</sup> In case of a recommendation on the adoption of a guideline, Article 37(2) of the Articles of Association excludes the representatives of the Founding Industry Members and the Industry Members from voting.<sup>313</sup> Should a two-thirds majority not be obtainable, the decision will be taken by unanimity of the representatives of the Founding Regulatory Members.<sup>314</sup>

The decision of the Assembly on the adoption of a guideline is also, in principle, taken by consensus.<sup>315</sup> However, at this stage only the members representing regulators are

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Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21.

<sup>309</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 21.

<sup>310</sup> ICH, ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 22.

<sup>311</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(4).

<sup>312</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(7).

<sup>313</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(2).

<sup>314</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 37(7).

<sup>315</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(2).

considered to be relevant for the forming of the consensus.<sup>316</sup> Again, before the actual voting takes place, the members that represent regulators will be asked to present their views. The Chair will take a decision on whether consensus will be achievable or whether the Assembly shall proceed with voting on a topic.<sup>317</sup> Where consensus cannot be achieved and the Assembly has to take a vote on the proposal, the Founding Industry Members and the Industry Members are excluded from the voting.<sup>318</sup> In this case a simple majority of the votes exercised by the Founding Regulatory Members, Standing Regulatory Members and Regulatory Members, which needs to include the votes of all Founding Regulatory Members, will be necessary for the adoption of a new topic for harmonisation in an ICH guideline.<sup>319</sup>

*Step 5* consists of regulatory implementation by the regulatory members.<sup>320</sup> The regulatory authorities will report the implementation measures taken to the Assembly and they will be published on the ICH website by the Secretariat.<sup>321</sup> The implementation of ICH guidelines in the EU is discussed extensively in Chapter 5.

Currently over 60 ICH guidelines have been adopted.<sup>322</sup> It is an ‘impressive’ result according to participants in the process.<sup>323</sup> Only one guideline (Q1F) has been withdrawn in the history of ICH harmonisation. The Q1F guideline harmonised storage conditions for regions with a humid climate (which are essentially non-ICH regions), and was withdrawn to leave the definition of these requirements to the respective regions and/or the WHO.<sup>324</sup> Moreover, only in the case of two harmonisation topics – the guideline on Data Elements and Standards for Drug Dictionaries (M5), and the guidelines on Virus and Gene Therapy Vector Shedding and Transmission (M6) – was the decision-making process stopped without culminating in the adoption of a guideline.<sup>325</sup>

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<sup>316</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>317</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 16.

<sup>318</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 9(2)(a) and Art. 12(2)(b).

<sup>319</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 25(5).

<sup>320</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 23.

<sup>321</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 23.

<sup>322</sup> A list of the guidelines adopted by the ICH until 19 March 2015 can be found in the Annex. Furthermore, information on the ICH guidelines and their status in the decision-making process can be found at: <http://www.ich.org/products/guidelines.html>, last accessed: 3 April 2017.

<sup>323</sup> Sauer (2013), p. vii.

<sup>324</sup> [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/-Quality/Q1F/Q1F\\_Explanatory\\_Note.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/-Quality/Q1F/Q1F_Explanatory_Note.pdf), last accessed: 3 April 2017.

<sup>325</sup> <http://www.ich.org/products/guidelines/multidisciplinary/article/multidisciplinary-guidelines.html>, last accessed: 3 April 2017.

Overall, it is worth repeating that consensus is the core decision-making principle of the ICH procedure. Nonetheless, within the formal decision-making process, not all members have the same prerogatives. On the one hand, the Founding Regulatory Parties both in the Management Committee and the Assembly have a protruding position, as their votes are always required to achieve a decision-making majority. On the other hand, both the Founding Industry Members as well as the Industry Members are curtailed in their powers to influence final decisions on the choice of harmonisation topics, as well as on the adoption of ICH guidelines. The role of industry representatives in the decision-making process has in particular only been subject to reform in the recent past; therefore, the next section will examine the changes in the ICH decision-making process through the reform in more detail.

#### 4.2 *Changes to the decision-making procedure over time: more regulator-driven*

In the standard-setting process leading to the adoption of ICH guidelines as described above, the industry representatives – both of the Founding Industry Members and Industry Members – play an important role. They participate in the Expert Working Groups responsible for forming the scientific consensus, which leads to a large influence of industry representatives on the content of the ICH guidelines. However, it has also been shown that in the final decisions on the adoption of the guidelines, the industry representatives are not considered for the forming of consensus in the Assembly, and cannot take part in the voting in both the Management Committee and the Assembly. However, the standard-setting procedure as described above has not always been carried out in this mode. The role of the industry parties has, in particular, been subject to reform in the recent past.

From the inception of the ICH until the reform, the ICH took its decision on the adoption of ICH guidelines in the Steering Committee, consisting of the regulators of the EU, US and Japan, as well as the industry representatives of these members.<sup>326</sup> As the decisions were taken by consensus, the industry used to be an equal partner in the decision-making process and essentially a co-regulator. With regard to the adoption of the final guideline, the members of the Steering Committee agreed if there was consensus, and subsequently the three regulatory parties signed off on the guidelines for adoption in their regions.<sup>327</sup> If one of the industry association representatives had objections because the final draft was diverging too far from the Expert Working Group draft as agreed upon between the parties, the regulatory parties could re-submit the draft to the EWG for renewed consideration.<sup>328</sup> Conducting the harmonisation process in this way essentially amounted to granting the industry a safeguard, which – subject to agreement of the regulators – allowed the industry to renegotiate the changes that have been introduced by the stakeholder consultation procedure.

Some changes to the procedure for ICH guideline adoption were agreed upon in June 2012, during the Steering Committee meeting in Fukuoka (Japan), in an effort to ‘better define the role of regulator and industry parties within the ICH’,<sup>329</sup> and to underline ‘that the regulators have the ultimate responsibility in ensuring the protection of public health’.<sup>330</sup> Moreover, the recent ICH reform also aimed at making the decision-making process more regulator-driven.<sup>331</sup>

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<sup>326</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 14.

<sup>327</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 14.

<sup>328</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 14.

<sup>329</sup> ICH, Press Release – ICH Steering Committee, Fukuoka, Japan, 6-7 June 2012.

<sup>330</sup> ICH, Press Release – ICH Steering Committee, Fukuoka, Japan, 6-7 June 2012.

<sup>331</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

In 2012, a change to the standard-setting process introduced the possibility that a Concept Paper could also be adopted if the industry parties did not agree with starting a harmonisation initiative for a specific topic.<sup>332</sup> This constraint on the influence of industry members on the choice of ICH topics entailed the possibility that, where consensus on the endorsement of a topic for harmonisation could not be reached in the Steering Committee, the regulatory parties could decide to nonetheless adopt a topic for harmonisation.<sup>333</sup> Moreover, a clearer borderline was introduced, between the forming of scientific consensus in a Technical Document, and the drafting of a regulatory guideline from *step 2b* onwards as responsibility of the regulatory parties.<sup>334</sup> This is signified also by the rule that after *step 2b* the Expert Working Group rapporteur has to be a representative of the regulatory parties. However, the core principle of the ICH harmonisation process remained consensus decision-making, a fact that was also not changed through the procedural changes initiated in Fukuoka.<sup>335</sup> Thus, these changes only relativised the industry influence on ICH decision-making to a certain extent, as through the consensus decision-making the industry still heavily influenced the guideline-forming.

Now, after the extensive procedural and institutional reform of the ICH, the influence of the industry on ICH guidelines has been further curtailed. Although consensus remains the core decision-making principle, the role of the industry has been further delimited. The industry is represented in the Expert Working Groups and, therefore, does influence the content of the ICH guidelines. In the initial step of choosing a topic for harmonisation, the industry representatives in the Management Committee take part in the decision-making on the recommendation. Where the decision on the adoption of a topic for harmonisation is then taken by the Assembly, the views of the industry are taken into account for forming a consensus. However, the Founding Industry Members and Industry Members are excluded from voting if consensus cannot be reached.

Moreover, where the scientific consensus in form of a Technical Document is agreed upon, for decisions in *step 2b* regarding the adoption of a Draft Guideline and *step 4* regarding the adoption of a final ICH guidelines, the industry representatives views are not taken into account for the forming of consensus in the Assembly and Founding Industry Members. Industry Members are also excluded from voting if consensus on the adoption cannot be achieved. In the Management Committee too, which adopts a recommendation for the Assembly on the adoption of a guideline, the industry representatives are excluded from voting if consensus cannot be achieved. Overall the reform and adoption of the Articles of Association, as well as the Rules of Procedure of the Assembly, have significantly contributed to clarifying how consensus decision-making in a more regulator driven ICH can be structured, and how decisions should be taken when consensus cannot be achieved.

Nonetheless, it should be stressed that although industry influence has been curtailed in the decision-making steps where consensus cannot be reached, this has not changed the significant influence of the industry on the forming of the content of the guidelines, which takes place on the level of the Expert Working Groups. Thus, whereas the decision-making process might now be more regulator-driven, the substance of the guidelines still comes into being in a co-regulatory effort between regulatory and industry experts. Therefore, in theory, the new rules give industry representatives less influence on the adoption of ICH guidelines, whereas they still contribute extensively to their substance in the Expert Working Groups.

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<sup>332</sup> ICH, Press Release – ICH Steering Committee, Fukuoka, Japan, 6-7 June 2012.

<sup>333</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 11.

<sup>334</sup> ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, p. 12f.

<sup>335</sup> ICH, Press Release – ICH Steering Committee, Fukuoka, Japan, 6-7 June 2012.

## 5. ASSESSING THE ICH'S LEGAL NATURE: PRE- AND POST-REFORM

The reform of the ICH and its legal establishment as an association under Swiss law meant that the ICH has undergone considerable changes in terms of its legal formalisation and also its institutional structure. Whereas the ICH used to be a meeting-based body, lacking any formal legal establishment, with the reform the legal nature of the ICH has been clarified. It is now an association under Article 60 et seq of the Swiss Civil Code, a body established under private law.<sup>336</sup> Moreover, according to its Articles of Association, the ICH is an international non-profit association.<sup>337</sup> The following section will assess the increasing formalisation of the legal nature of the ICH, and question whether a status as private body fully encapsulates the legal nature of the ICH.

5.1 *ICH pre-reform: a lack of legal establishment*

Before the recent reform, the ICH itself did not provide any information on its legal nature and preferred to refer to itself as a 'joint regulatory/ industry project',<sup>338</sup> which is devoid of legal meaning. At its inception the ICH lacked a treaty basis, which would legally establish it under international law, and was also not legally established under the law of one of the members.

When founding the ICH, the parties refrained from formally establishing the ICH as an international organisation through an international treaty or other legal act, and they consequentially also did not confer international legal personality to their initiative. The fact that the ICH founders deviated from the establishment as an international organisation needs to be seen in the wider context of developments, with regard to a broadening of the spectrum of bodies taking on regulatory tasks at the global level, as described in Chapter 1.<sup>339</sup> In this regard it was discussed that global standard-setting not only takes place within international organisations, but also in other bodies, such as transnational regulators networks, private standard-setting bodies and public-private partnerships.

One factor that probably withheld the founders from establishing an international organisation is that the ICH was intended to be a temporarily limited initiative, to be terminated once the harmonisation was carried out, which was estimated to need six years.<sup>340</sup> Moreover, international organisations traditionally do not provide the possibility of having private parties as full members on a par with states, due to the debated legal personality of international non-governmental organisations (INGOs). Overall, the fact that the founding parties deviated from the establishment of an international organisation in the setting up of the institutional framework of their harmonisation initiative is a reflection of the shift from government to governance on the global level, leading to a variety of actors and forms of

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<sup>336</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 1(1).

<sup>337</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 2(1).

<sup>338</sup> ICH, The Future of ICH – Revised 2000 – Statement by the ICH Steering Committee on the occasion of the Fifth International Conference on Harmonisation, 9-11 November 2000, San Diego, p. 1 (the information has now been removed from the website. A copy is on file with the author).

<sup>339</sup> Chapter 1, Section 4.2.

<sup>340</sup> Katsikas (2011), p. 89. See also: Berman (2011a), p. 18.

organisation that traditional international law is not able to grasp.

The ICH was not organised as a permanent institution but operated largely on a meeting basis in 6-monthly intervals. With its organisational format, the ICH resembled a network.<sup>341</sup> Like the ‘transnational regulators networks’ discussed in Chapter 1, which constitute an informal format of cooperation of national administrative regulators, the ICH also lacked a legal basis and legal personality, but operated on the basis of recurring meetings of the Steering Committee and the working groups, with the six founding members interacting as equals, sharing resources, while lacking a strict organisational plan.<sup>342</sup> However, whereas per definition the members of these transnational regulators networks are public parties, since they are representatives of national regulatory authorities, the ICH also integrated the regulated industry as members. Therefore, even before the reform the ICH was qualified as a ‘public/private platform’<sup>343</sup> or ‘public-private collaboration’,<sup>344</sup> and ‘public-private network’.<sup>345</sup> It thus formed a public-private partnership in the organisational format of a network.<sup>346</sup>

It has to be stressed that although the ICH operated under a rather informal meeting format, these network structures are not to be underestimated with regard to their actual influence on global governance. The participation in networks has been shown to lead to high compliance with the norms established by that network, and will eventually also lead to the convergence of regulatory systems through cooperation.<sup>347</sup> Nonetheless, it should be noted that this lack of legal personality had the downside that the ICH was not capable of entering into a legal relationship, like contracts. Therefore a contract with the Support Services Organisation (MSSO) that carries out the day-to-day work regarding the maintenance and advancement of the medical dictionary MedDRA had to be concluded by the IFPMA acting as ‘trustee’ of the Steering Committee. This problem has been overcome through the recent reform with the establishment of the ICH under Swiss law.

## 5.2 ICH post-reform: a public-private partnership established as association under Swiss law

Chapter 1 introduced a typology of global standard-setting bodies, which distinguished four types of bodies: international organisations, transnational regulators networks, private standard-setting bodies, and public-private partnerships.<sup>348</sup> Whereas the ICH was organised as a network before its reform, it has now evolved into a body with legal personality under national law: an international non-profit association under Swiss law. According to the ICH, the legal establishment of the ICH under Swiss law will ‘give ICH a more stable operating structure’.<sup>349</sup> While the ICH now is established as a private body in form of a Swiss

<sup>341</sup> For other discussions on the ICH network character see: Spina (2011), pp. 249-268; A. Berman, ‘Public-Private Harmonization Networks: The Case of the International Conference on Harmonization (ICH)’, in S. Cassese, B. Carotti, L. Casini, E. Cavalieri & E. MacDonald (Eds.), *Global Administrative Law: The Casebook*, 3<sup>rd</sup> Edition (2012b), pp. 228-234, available via: <http://www.irpa.eu/wp-content/uploads/2012/08/The-Casebook-Chapter-1.pdf>, last accessed: 3 April 2017.

<sup>342</sup> Chapter 1, Section 4.

<sup>343</sup> Spina (2011), p. 258.

<sup>344</sup> Berman (2011a), p. 3.

<sup>345</sup> Ibidem.

<sup>346</sup> On the different organizational formats of PPP’s see: Chapter 1, Section 4.2.4.

<sup>347</sup> Slaughter & Zaring (2006), p. 215.

<sup>348</sup> Chapter 1, Section 4.2.

<sup>349</sup> ICH, Press Release – ICH announces organisational changes as it marks 25 years of successful harmonisation, Geneva, 26 October 2015.

association, the previously discussed membership, institutional structure and decision-making process, have all shown that the principal characteristic of the ICH remains the fact that it combines regulators and industry in a body with regulatory power.

Public-private partnership was introduced in Chapter 1 as an umbrella term that does not correlate to a certain legal establishment of a body, but is used in legal scholarship to describe a range of bodies characterised by the cooperation of public and private parties.<sup>350</sup> This mix of governmental and non-governmental members has been termed ‘hybridity’.<sup>351</sup> Public-private partnerships are defined by the cooperation of public (regulatory or governmental) and private (profit or not-for-profit organisations) parties.<sup>352</sup> As a regulator and industry cooperative harmonisation initiative, the ICH appears to fit squarely into this definition. Moreover, it was pointed out that the partners in a PPP habitually undertake joint decision-making and, furthermore, that PPPs are characterised by shared rights and responsibilities between the actors.

Given the broad organisational spectrum that the umbrella term public-private partnership covers, the establishment as a private association under Swiss law does not hinder the qualification of the ICH as a public-private partnership as such.<sup>353</sup> This is especially since according to the new Articles of Association, the ICH remains public-private in character, with representatives of regulators and Regional Harmonisation Initiatives on the one hand, and representatives of industry associations and industry organisations on the other hand.<sup>354</sup> However, it should be assessed whether the partnership between regulators and industry that was established for the ICH pre-reform is still intact after the changes to the institutional structure, the decision-making process and the funding of the ICH; a statement from the ICH Steering Committee proclaimed that reforms will be undertaken towards the ‘introduction of greater clarity regarding the distinct and separate roles of the ICH regulatory and industry parties in ICH’.<sup>355</sup>

With regard to the institutional structure of the ICH, public as well as private parties participate in the two main governing bodies. In the Assembly each member is entitled to two representatives, which guarantees the participation rights of both public and private bodies.<sup>356</sup> In the Management Committee consisting of 28 Members, 10 representatives will be industry representatives and 18 will be regulatory members, which means that although there is representation of industry interests in the Management Committee, the majority of the members will be public member representatives.<sup>357</sup> Thus, public as well as private parties are represented in the main governing bodies of the ICH.

As the membership applications are still ongoing it is unclear if there will be an equilibrium of public and private members in the Assembly. Currently, the applications for membership have only just started.<sup>358</sup> Thus, it remains to be seen whether the equilibrium of public and private parties within the ICH will persevere, given that the aim of the reform was to make the ICH more regulator-focused and to open up to other regulators, while it of

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<sup>350</sup> Chapter 1, Section 4.2.4.

<sup>351</sup> See e.g.: Kingsbury, Krisch & Stewart (2005), pp. 15-62; L. Casini, “‘Down the Rabbit Hole’”: The Projection of the Public/Private Distinction Beyond the State’, New York University School of Law, Jean Monnet Working Paper No. 8/2013, (2013); M. Ruffert & C. Walter (Eds.), *Institutionalisiertes Völkerrecht* (München: Verlag C.H. Beck, 2009), p. 8.

<sup>352</sup> Chapter 1, Section 4.2.4.

<sup>353</sup> Chapter 1, Section 4.2.4.

<sup>354</sup> Section 2 and Section 3.

<sup>355</sup> ICH, Press Release – ICH Steering Committee, Minneapolis, MN, USA, June 2014.

<sup>356</sup> Section 3.2.1.

<sup>357</sup> Section 3.2.2.

<sup>358</sup> <http://www.ich.org/about/membership.html>, last accessed: 3 April 2017.

course also provides room for including other industry associations that are affected by ICH guidelines.<sup>359</sup> However, the focus seems to be on an extension of regulatory members rather than industry members, as also becomes evident from the ICH website: ‘More involvement from regulators around the world is *welcomed and expected* (...). This is matched by the *possibility* of wider inclusion of global industry sectors affected by ICH harmonisation.’<sup>360</sup>

For the standard-setting process as such, it was clarified that the process became more regulator-driven, since the industry representatives have lost their say in the actual adoption of ICH guidelines.<sup>361</sup> However, it has also been clarified that industry representatives remain an integral part of the forming of the scientific consensus in the Expert Working Groups.<sup>362</sup> Yet what will change substantially is the funding of the ICH, as it will be membership fee-based, while the attendance of the ICH meetings will be covered by the respective party itself.<sup>363</sup> Nonetheless, as the amount of the membership fee will be determined by the ICH Assembly and may vary for the different categories of members, it remains to be seen whether the burden will be shared equally between regulatory and industry members.<sup>364</sup>

Conclusively, the ICH will still be characterised by its public-private membership, with a co-regulatory decision-making process, as well as the sharing of expertise and financial resources of the regulators and the industry associations. Therefore, the ICH is to be qualified as a public-private partnership, although after the reform it has been legally established under Swiss law.

The establishment of an Association under the reform process did not only introduce a valuable clarification on the legal establishment of the ICH as such, but the Articles of Association also entail provisions that further clarify legal aspects of the ICH as an association. Article 60 deals with a potential conflict of laws that could arise for members between the Articles of Association of the ICH and the laws under which this specific member is established. The Article determines that in such conflict, the laws of the legal system under which the respective member is organised prevail over any obligations under the ICH Articles of Association. Furthermore, the Articles of Association contain a clause on liability, through which liabilities and obligations are limited to the Association as such, and may not be extended to a personal liability of any member or person acting on behalf of a member in the ICH.<sup>365</sup> However, in cases of gross negligence or intent, the Association and its Members might hold an individual acting in the ICH liable,<sup>366</sup> which is due to the fact

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<sup>359</sup> Lenita Lindström-Gommers, Presentation at the 76th Pharmaceutical Committee, 28 April 2016, via: [http://ec.europa.eu/health/files/committee/76meeting/-pharm710\\_5ai\\_ich\\_reform\\_presentation.pdf](http://ec.europa.eu/health/files/committee/76meeting/-pharm710_5ai_ich_reform_presentation.pdf), last accessed: 3 April 2017.

<sup>360</sup> ICH, Press Release – ICH announces organisational changes as it marks 25 years of successful harmonisation, Geneva, 26 October 2015 (emphasis added).

<sup>361</sup> Section 4.

<sup>362</sup> Section 4.

<sup>363</sup> Section 2.4.

<sup>364</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 58.

<sup>365</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 61.

<sup>366</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 61(2).

that under Swiss law, personal liability cannot be excluded in these cases.<sup>367</sup>

The introduction of a dispute resolution mechanism in Article 63 of the Articles of Association is also remarkable, and is further clarified in the Rules of Procedure of the Assembly. Here it was determined that disputes between the ICH and its members will be referred to an outside legal counsel by the Chair of the Assembly, which will perform the function of a mediator in arising disputes.<sup>368</sup> Where the outside legal counsel is not successful in finding a solution, it will report to the Assembly which decides if it is possible to resolve the dispute or, upon proposal of the Management Committee,<sup>369</sup> appoints a Dispute Resolution Board consisting of three representatives of the regulatory members, including one Funding or Standing Regulatory Member as Chair.<sup>370</sup> Where a Dispute Resolution Board is formed, it will take a decision by the majority of its members.<sup>371</sup> The legal effect of such a decision is, however, not clarified in the Rules of Procedure.

## 6. ICH GUIDELINES UNDER SCRUTINY

Finally, a presumption that has been carried through the prior parts of this chapter needs to be verified: up until now the ICH guidelines have been presented as standards, without further questioning this assumption. Therefore, in order to validate this presumption, the definition of ‘standard’ as established in the first Chapter is recalled, where standards are defined as voluntary expertise-based rules constituting measurable criteria, by which a product or a production process or service can be evaluated on the basis of technical or physical conditions.<sup>372</sup>

As addressed previously, the ICH guidelines constitute recommendations, which are implemented into the national regulatory systems, while the guidelines as such are lacking legally binding force.<sup>373</sup> They serve the assessment of medicinal products. On the one hand, they address the regulatory authorities that are members of the ICH, where they will be used to evaluate marketing authorisation applications. On the other hand, they regulate the activities of the research-based pharmaceutical industry, which will have to make sure their products and production as well as testing processes will conform to ICH guidelines, in

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<sup>367</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 27.

<sup>368</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 27.

<sup>369</sup> If a member of the Management Committee is involved in the dispute, no proposal is required. ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 27.

<sup>370</sup> If a Founding Regulator Member is involved in the dispute, the Chair should be a Standing Regulatory Members. ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 27f.

<sup>371</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 28.

<sup>372</sup> Chapter 1, Section 2.2.

<sup>373</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 3.

order to get them authorised in the countries that use the standards. Moreover, they lay down measurable criteria, determining aspects of quality, safety and efficacy of medicinal products, such as the duration of toxicity tests (ICH S4) or statistical principles for the design of clinical trials (ICH E 9). They thus constitute standards within the definition used in this research.

Having established that ICH guidelines can be defined as standards, it is now time to examine the types of standards the ICH sets and inquire into their legal nature.

### 6.1 ICH guideline categorisation

The ICH guidelines adhere to a division into quality, safety and efficacy topics, reflecting the core criteria for scientific assessment in the marketing authorisation procedure for medicinal products.<sup>374</sup> In addition to these three categories, a ‘multidisciplinary’ category was created for topics that do not fit well into (only) one of the above categories.

As the name suggests, *quality guidelines* contain methods to ensure the quality of a pharmaceutical product. For example, they are concerned with establishing test methods to guarantee that the products maintain the same quality throughout their shelf life. Therefore the Q1A guideline contains testing standards establishing the duration, temperature and humidity under which the shelf life of a product is tested.<sup>375</sup> This is complemented with the Q1B guideline for testing the photostability of new substances, thus, whether the exposure to light will have an effect on their quality.<sup>376</sup> Moreover, there are guidelines dealing with the impurities in drug substances (Q3A-D),<sup>377</sup> or establishing guidance for testing new drug substances (Q6A<sup>378</sup> and Q6B<sup>379</sup>). Importantly, the manufacturing of pharmaceuticals is also harmonised through the Q7 guideline, dealing with the Good Manufacturing Practice.<sup>380</sup>

The *safety guidelines* address potential risks in the form of toxic effects of the product. Topics harmonised are, for example, carcinogenicity studies (S1A-S1C),<sup>381</sup> which contains rules for testing on cancer-causing properties, or genotoxicity studies (S2),<sup>382</sup> concerned with testing for negative effects on genetic material. Tests on whether a drug will cause birth

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<sup>374</sup> Kuhnert (2011), p. 17.

<sup>375</sup> ICH, ICH Harmonised Tripartite Guideline – Stability Testing of New Drug Substances and Products Q1A(R2), 6 February 2003.

<sup>376</sup> ICH, ICH Harmonised Tripartite Guideline – Stability Testing: Photostability Testing of New Substances and Products – Q1B, 6 November 1996.

<sup>377</sup> ICH, ICH Harmonised Tripartite Guideline – Impurities In New Drug Substances Q3A(R2), 25 October 2006; ICH, ICH Harmonised Tripartite Guideline – Impurities In New Drug Products Q3B(R2), 2 June 2006; ICH, ICH Harmonised Tripartite Guideline – Impurities: Guideline For Residual Solvents Q3C(R5), 4 February 2011; ICH, ICH Harmonised Tripartite Guideline – Guideline For Elemental Impurities Q3D, 16 December 2014.

<sup>378</sup> ICH, ICH Harmonised Tripartite Guideline – Specifications: Test Procedures And Acceptance Criteria For New Drug Products: Chemical Substances Q6A, 6 October 1999.

<sup>379</sup> ICH, ICH Harmonised Tripartite Guideline – Specifications: Test Procedures And Acceptance Criteria For Biotechnological/Biological Products Q6B, 10 March 1999.

<sup>380</sup> ICH, ICH Harmonised Tripartite Guideline – Good Manufacturing Practice Guide For Active Pharmaceutical Ingredients Q7, 10 November 2000.

<sup>381</sup> ICH, ICH Harmonised Tripartite Guideline – Guideline On The Need For Carcinogenicity Studies of Pharmaceuticals S1A, 29 November 1995; ICH, ICH Harmonised Tripartite Guideline – Testing for Carcinogenicity Of Pharmaceuticals S1B, 16 July 1997; ICH, ICH Harmonised Tripartite Guideline – Dose Selection For Carcinogenicity Studies of Pharmaceuticals S1C(R2), 27 October 1994.

<sup>382</sup> ICH, ICH Harmonised Tripartite Guideline – Guidance On Genotoxicity Testing And Data Interpretation For Pharmaceuticals Intended For Human Use S2(R1), 9 November 2011.

defects or might have a negative effect on fertility are also established in an ICH guideline (Reproductive Toxicology S5).<sup>383</sup> Moreover, a special guideline is established for the safety of biotechnological products (S6).<sup>384</sup>

*Efficacy guidelines* address the clinical trials that have to be conducted in order to obtain a marketing authorisation for a medicinal product. Clinical trials are the phase in the drug development process where the drug is tested on humans. Various aspects of clinical trials are regulated in ICH guidelines, such as the definition of terminology used to collect and report the results of clinical trials (for example a harmonised definition of Adverse Event or Adverse Drug Reaction), in the ICH E2A Guideline.<sup>385</sup> Moreover, the ICH agreed on a Good Clinical Practice Guidance (E6), which is meant to ensure that the clinical trials result are reliable, and that the participants in clinical trials are adequately protected through establishing ‘an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.’<sup>386</sup> The E5 Guideline on Ethnic Factors in Clinical Trials Data has also been an important contribution to pharmaceutical standards as it facilitates the acceptance of clinical trials conducted in a country that is not the country where marketing authorisation is requested.<sup>387</sup> This is highly relevant as it significantly reduces the number of clinical trials necessary to be conducted. Agreement on this issue was complicated through the fact that in drug regulation, ‘factors relating to the genetic and physiologic (intrinsic) and the cultural and environmental (extrinsic) characteristics of a population’<sup>388</sup> need to be taken into account.

Interestingly, the efficacy guidelines not only contribute to the regulation of data necessary for the marketing authorisation of pharmaceuticals, but also contribute significantly to the harmonisation of pharmacovigilance requirements. Pharmacovigilance is concerned with gathering data on, analysing and reacting to the adverse effects of pharmaceuticals when they are already marketed.<sup>389</sup> Although the E2A on definitions and standards for expedited reporting is concerned with adverse drug reactions in the clinical trials conducted before the marketing of a product,<sup>390</sup> it has also been applied to pharmacovigilance activities after the marketing authorisation has been granted.<sup>391</sup> With the

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<sup>383</sup> ICH, ICH Harmonised Tripartite Guideline – Detection of Toxicity To Reproduction For Medicinal Products & Toxicity To Male Fertility S5(R2), 24 June 1993. See: Jordan (1992), p. 494.

<sup>384</sup> ICH, ICH Harmonised Tripartite Guideline – Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals S6(R1), 16 July 1997.

<sup>385</sup> ICH, ICH Harmonised Tripartite Guideline – Clinical Safety Data Management: Definitions And Standards For Expedited Reporting E2A, 27 October 1994.

<sup>386</sup> ICH, ICH Harmonised Tripartite Guideline – Guideline For Good Clinical Practice E6, 10 June 1996, p. 1.

<sup>387</sup> ICH, ICH Harmonised Tripartite Guideline – Ethnic Factors In The Acceptability For Foreign Clinical Data E5(R1), 5 February 1998. See: J. Molzon, A. Giaquinto, L. Lindstrom, T. Tominaga, M. Ward, P. Doerr, L. Hunt & L. Rago, ‘The Value and Benefits of the International Conference on Harmonisation to Drug Regulatory Authorities: Advancing Harmonization for Better Public Health’, 89(4) *Clinical Pharmacology & Therapeutics* (2011), pp. 503-512, p. 508.

<sup>388</sup> ICH, ICH Harmonised Tripartite Guideline – Ethnic Factors In The Acceptability For Foreign Clinical Data E5(R1), 5 February 1998, p. 1.

<sup>389</sup> G. Castle & B. Kelly, ‘Global Harmonization Is Not All That Global: Divergent Approaches in Drug Safety’, 63(3) *Food and Drug Law Journal* (2008) pp. 601-622, p. 601. See also: Spina (2011), p. 255.

<sup>390</sup> ICH, ICH Harmonised Tripartite Guideline – Clinical Safety Data Management: Definitions And Standards For Expedited Reporting E2A, 27 October 1994.

<sup>391</sup> Bahri & Tsintis (2005), p. 379.

E2D guideline on post-approval safety data management, the ICH finally adopted a guideline explicitly devoted to the post-authorisation phase.<sup>392</sup> Overall, the ICH has been very influential in the pharmacovigilance processes of its members.<sup>393</sup>

Finally, as a fourth type of ICH standard, the multidisciplinary guidelines are a ‘catch-all’ category that encompass guidelines which do not fit into a single of the above described categories. Here, the most relevant guidelines are the M4 guidelines establishing the Common Technical Document (CTD).<sup>394</sup> The CTD/eCTD is a harmonised format for the marketing authorisation application, and will be closely examined with regard to its structure and impact in Chapter 5, dealing with the implementation of ICH guidelines in the EU.<sup>395</sup>

## 6.2 *Legal status of ICH guidelines*

Having set out the process of standard-setting within the ICH and the categories of guidelines, now the guidelines will be assessed with regard to their legal nature. While the following will look at the legal status of the outcome of the ICH process, before the rules are implemented by the regulators represented in the ICH, Chapter 5 is devoted to the assessment of the legal status of the guidelines once they are implemented in the European Union.

As for the legal status of ICH guidelines, the reform and especially the adoption of the Articles of Association and the Rules of Procedure of the Assembly have contributed to clarifying how the ICH itself assesses the legal nature of its standards. First of all, the Articles of Association lay down that the Founding Regulatory Members, the Standing Regulatory Members, and the Regulatory Members ‘are expected to implement all ICH Guidelines in accordance with the applicable Rules of Procedure’.<sup>396</sup> The Founding Industry Members will ‘actively support and encourage the compliance by the Founding Industry Member and/or its affiliated members with the ICH Guidelines’,<sup>397</sup> and the Industry Members will ‘actively support and encourage the compliance with the ICH Guidelines that the Industry Member

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<sup>392</sup> ICH, ICH Harmonised Tripartite Guideline – Post-Approval Safety Data Management: Definitions And Standards For Expedited Reporting E2D, 12 November 2003.

<sup>393</sup> Bahri & Tsintis (2005), pp. 377-387.

<sup>394</sup> ICH, ICH Tripartite Guideline – Organisation Of The Common Technical Document For The Registration Of Pharmaceuticals For Human Use M4, 5 June 2016; ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Quality – M4Q(R1) – Quality Overall Summary Of Module 2 And Module 3: Quality, 12 September 2002; ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Safety – M4S(R2) – Overview And Nonclinical Summaries Of Module 2 – Organisation Of Module 4, 20 December 2002; ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Efficacy – M4E(R1) – Overview And Clinical Summary Of Module 2- Module 5 Clinical Study Reports, 12 September 2002.

<sup>395</sup> Chapter 5, Section 3.2.

<sup>396</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 8(5) for Founding Regulatory Members, Art. 10(4) for Standing Regulatory Members, Art. 11(5) for Regulatory Members.

<sup>397</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 9(3)(b).

or its affiliated members are regulated or affected by'.<sup>398</sup> Thus, the members representing regulators should implement the guidelines, while the members representing industry associations are responsible for promoting the use of ICH guidelines in the associations and the companies they represent. However, the Articles of Association do not contain a legally binding obligation for the members to implement ICH guidelines and, furthermore, characterise the guidelines as 'recommendations towards achieving greater harmonisation'.<sup>399</sup> This is confirmed in the Rules of Procedure of the Assembly, which explicitly state that the ICH guidelines are not legally binding.<sup>400</sup> As Fernand Sauer, former Executive Director of the EMA and founding member of the ICH explains: 'ICH has no authority to impose regulatory requirements (...). It can only advise regulators and regulated on scientific issues.'<sup>401</sup>

Since the inception of the ICH, the commitment of the members to implement the guidelines regardless of their voluntary character has been emphasised. During the ICH's second Steering Committee meeting of October 1990, the parties firmly expressed their 'commitment to increased international harmonisation'.<sup>402</sup> And indeed, before the reform of the ICH, when the regulators of the EU, US and Japan were the only regulatory members of the ICH, the guidelines were implemented without fail in the regulatory framework of the EU, US and Japan.<sup>403</sup> It is indeed the commitment of the ICH regulatory parties to implement the guidelines endorsed in the ICH process that has contributed to the success of the ICH over the years.<sup>404</sup> The fact that the implementation has been reliably carried out by the three original regulatory parties to the ICH before the reform, has built a system of mutual trust.<sup>405</sup> A Commission official has described this commitment as a 'gentlemen's agreement': that once the regulator signs off the guideline at *step 4*, this regulator has committed to implementing the guideline.<sup>406</sup> Thus, the guidelines are not implemented due to a legal obligation, but rather due to a political commitment and group dynamic that has

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<sup>398</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 12(3)(b).

<sup>399</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 3(a).

<sup>400</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 3.

<sup>401</sup> Sauer (2013), p. viii.

<sup>402</sup> ICH, Statement by the ICH Steering Committee Tokyo, October 1990, available at: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Vision/ICH\\_SC\\_Statement\\_1990.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Vision/ICH_SC_Statement_1990.pdf), last accessed: 3 April 2017.

<sup>403</sup> A list of the guidelines adopted by the ICH and their implementation in the EU can be found in the Annex. Furthermore, information on the implementation status can be found in the Guidelines section of the ICH website. <http://www.ich.org/products/guidelines.html>, last accessed: 3 April 2017.

<sup>404</sup> <http://www.ich.org/about/mission.html>, last accessed: 3 April 2017. Also confirmed by the Commission: Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>405</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>406</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

built up over the years. Therefore, although there is no legal obligation for the ICH members to implement the guidelines, the guidelines become *de facto* binding through the participation of ICH members in the process. In essence they are self-binding on the members.

Now, after the ICH reform, the membership of the ICH will be broadened and new regulators will join the ICH as Regulatory Members. As explained, these members should also implement the ICH guidelines according to the Articles of Association.<sup>407</sup> However, the new Regulatory Members are not expected to have implemented all ICH guidelines before they apply for membership. Instead, a gradual implementation of the guidelines is envisaged in three stages according to the importance of the guidelines.<sup>408</sup> First of all, in order to be eligible for the application to become a Regulatory Member, the ‘Tier 1 Guidelines’ Q1, Q7 and E6 have to be implemented by the respective regulator or the members of a Regional Harmonisation Initiative.<sup>409</sup> Where the application is successful and a regulator or Regional Harmonisation Initiative becomes a Regulatory Member, they will submit a plan with timeframes to implement the ‘Tier 2 Guidelines’ E2A, E2B, E2D, M4 and M1, aiming for implementation within five years.<sup>410</sup> The rest of the guidelines, the ‘Tier 3 Guidelines’, should be implemented ‘in the near term and as soon as possible’.<sup>411</sup> The implementation process is subject to oversight by the Assembly and will form a special agenda item in the meetings.<sup>412</sup> Therefore, although the flawless implementation rate of the ICH prior to the reform is presumably endangered by the enlarged ICH membership, the reform process includes a structured approach to leading new members into implementing all ICH guidelines.

The voluntary nature of the ICH guidelines is also highlighted by the fact that the ICH has no internal enforcement mechanism to address incorrect or a lack of implementation. With regard to the implementation of ICH guidelines by new Regulatory Members, the Assembly Rules of Procedure provide that, where in exceptional circumstances a Regulatory Member only implements a guideline partially or cannot implement the guideline, it has to inform the ICH Secretariat and provide justifications.<sup>413</sup> However, no legal consequences are attached to a missing or solely partial implementation.

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<sup>407</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11(5).

<sup>408</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 3f.

<sup>409</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 11.

<sup>410</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 4.

<sup>411</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 4.

<sup>412</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 4.

<sup>413</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 4.

Overall, the ICH has a very successful history with regard to the implementation of its guidelines. The original three regulatory members have implemented all ICH guidelines; ICH guidelines implemented in non-member countries also triggered the ICH reform and its enlarged membership in the first place. Certainly consensus as a core principle in the decision-making process has contributed significantly to the successful implementation of the adopted guidelines in the past. As a guideline was only adopted when every regulatory party was satisfied with the consensus, the regulatory parties were also willing to implement it.<sup>414</sup> It is also argued in the literature that the dialogue nature of the standard-setting process and the decision-making by consensus are central to understanding the operation of the harmonisation process and its success.<sup>415</sup> That the ICH guidelines are a product of negotiated rule-making, means that the parties are more willing to accept the norms, since they have contributed to their development.<sup>416</sup> After the ICH reform, consensus remains the main decision-making principle, however, as explained before, the new Articles of Association provide that where consensus cannot be achieved voting will take place in both the Management Committee and the Assembly.<sup>417</sup> Whether this will affect the implementation of the guidelines can only be evaluated in the future, when enough experience with regard to the new decision-making practice is gathered. Moreover, it is not yet clear whether the voting on the adoption of a guideline will be a regular occurrence or if it will remain a rare exception.

However, apart from consensus as a trigger for implementation, other factors should be considered too. In the very scientific and technical area of pharmaceutical regulation in particular, the agreement on a standard as commonly accepted by the regulatory authorities and industry 'represents de facto a limitation of the discretionary power of administrative bodies at national level to deviate from the standards or to present a different assessment without a sound justification.'<sup>418</sup> This is caused by the scientific expertise represented in the ICH, which lends high persuasive power to a consensus of these highly qualified experts. Indeed, in general, international harmonisation through bodies like the ICH is often respected because these bodies are equipped with the leading experts in the respective fields, which gives their guidelines a high level of scientific authority.<sup>419</sup> The high scientific quality has been attested to the ICH in a WHO report.<sup>420</sup> This high scientific value provides the guidelines with authority and acceptance amongst ICH members as well as non-ICH members.

As discussed in Chapter 1, standards gain their effectiveness not from hierarchical coercion, but more so from the horizontal cooperation process through which they are adopted.<sup>421</sup> In this regard, the concept of soft law in international law as introduced in Chapter 1 also becomes relevant.<sup>422</sup> It was explained that legally non-binding measures can also be qualified as soft law, where they introduce certain obligations which (indirectly) affect the legal situation of a variety of actors, being capable of constraining the freedom to act of

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<sup>414</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>415</sup> Spina (2011), p. 263; Lezotre (2014), p. 61.

<sup>416</sup> Contrera (1994-1995), p. 937.

<sup>417</sup> Section 4.

<sup>418</sup> Spina (2011), p. 263.

<sup>419</sup> Wouters & Verhoeven (2005), p. 261.

<sup>420</sup> World Health Organization, *The Impact of Implementation of ICH Guidelines in Non-ICH Countries*, Report of a WHO Meeting 13-15 September 2001 (Geneva), Regulatory Support Series No. 9, WHO/EDM/QSM/2002.3, p. 15.

<sup>421</sup> Chapter 1, Section 2; Röhl (2007), p. 321; Möllers (2005a), p. 378.

<sup>422</sup> Chapter 1, Section 3.1.

the parties that agreed on the measure, conditioning their actions through their authority, thereby leaving the possibility to deviate to mere fiction.<sup>423</sup>

As the previous analysis has shown, the ICH adoption of ICH guidelines, before and after the reform process, leads to a commitment of regulatory parties to implement the agreed guidelines. Although this commitment is not legally enforceable, the decision-making process itself and the scientific authority of the guidelines de facto provide the ICH guidelines with a self-binding power regarding the signing regulators, and significantly diminish the possibility of deviating from the agreed scientific consensus. In the case of ICH guidelines therefore it has to be concluded that they constitute soft law.

## 7. CONCLUSION

Today, the ICH is the dominant source of pharmaceutical standards. The ICH aims at the harmonisation of the regulatory requirements for the quality, safety and efficacy of medicinal products, and in this context has adopted over 60 guidelines.

Through its reform the ICH has undergone a significant change, while the reform process was triggered through the increasing influence of ICH guidelines on non-ICH countries. This first led to institutional changes in the ICH, like the creation of the Global Cooperation Group, which was succeeded by the Global Cooperation session in the Steering Committee agenda. With the reform, full membership can be accorded to drug regulatory authorities, regional harmonisation initiatives, and industry associations. With regard to its institutional structure, the Assembly and the Management Committee have both replaced the Steering Committee as the main governing body, while the scientific consensus that is the basis of the guidelines is formed in Expert Working Groups. The ICH, therefore, operates a two-tier structure, characterised by the separation of management and final decision-making as opposed to the forming of the scientific consensus. In coordinating this process, the ICH strongly relies on its Secretariat.

While the ICH is now legally established as an Association under the Swiss Civil Code, it continues to be a public-private partnership characterised by the participation of regulatory and industry representatives on all institutional levels. In this regard, the ICH heavily depends on the expertise provided by both industry and regulators in order to form the guidelines. Moreover, although post-reform the ICH places a larger emphasis on the role of the regulators as being ultimately responsible for the protection of public health, the industry parties still decisively influence the guidelines. Thus, through the ICH process, the pharmaceutical industry has become a co-regulator of the products it produces.

The ICH guidelines are not legally binding standards, but it is recommended that the regulatory parties adopt them. Its members have implemented the guidelines without fail. This is due to their origin in horizontal cooperation, and the commitment of the parties to implement the outcome of a consensus forming process. Thus, although not legally binding, the guidelines are de facto binding upon the members and can be characterised as soft law.

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<sup>423</sup> Chapter 1, Section 3.2; von Bogdandy, Dann & Goldmann (2010), p. 11f.



## Chapter 5: Implementation of ICH standards in the EU

### 1. INTRODUCTION

Once International Council for Harmonisation (ICH) guidelines have been adopted on a global level, step 5 of the ICH decision-making procedure foresees that the ICH regulatory parties implement the standards agreed upon in their respective regulatory frameworks. Whereas the previous chapter assessed the ICH and Chapter 3 introduced the European pharmaceutical regulation, it is now time to assess the point where these two regulatory systems meet: the implementation of ICH guidelines in the European Union framework for pharmaceutical regulation. This chapter will analyse how precisely they are implemented, as well as how ICH standards affect this regulatory framework beyond their mere implementation.

In the EU, the European Medicines Agency (EMA) implements the ICH guidelines through adoption as EMA guidelines, subject to approval of the Committee for Medicinal Products for Human Use (CHMP), the main scientific committee of the agency. This implementation process is elaborated on in Section 2. The effect of this implementation on EU pharmaceutical regulation is discussed in Section 3. This includes a closer look at one of the most important ICH work products, the Common Technical Document (CTD), assessing its implementation and impact (Section 3.2). The influence of ICH guidelines on Commission guidance documents (Section 4.1), and European legislation (Section 4.2), and the case law of the Court of Justice of the European Union (Section 4.3) will also be examined.

The aim of this chapter is to provide a detailed account of the effects of ICH guidelines on the European regulatory framework for pharmaceuticals. It will analyse how deeply the norms set at the ICH level penetrate the European regulation. In this regard, the chapter exemplifies how global standards, which are voluntary, soft law measures when characterised under international law, shape the reality of risk regulation in the EU in practice.

### 2. IMPLEMENTATION OF ICH STANDARDS IN THE EUROPEAN UNION

It was established in Chapter 1 that where the EU concludes international agreements, these are binding upon the EU institutions and the Member States.<sup>1</sup> However, global standards, since they are not legally binding, require a connecting measure ('Bindungselement') to be incorporated into a regulatory framework.<sup>2</sup> In this regard, they can either be referenced in a binding legislative measure through a static or dynamic binding reference, or through an obligation to take the respective standards into account. Alternatively, the implementation can be carried out through the adoption of EU soft law measures such as administrative guidelines. The global standards are then adopted as guidelines by the Commission or agencies and form part of the administrative rule-making of these bodies. This route of implementation of global standards in the EU regulatory framework is illustrated in further detail below, where the implementation of ICH guidelines as EMA guidelines adopted by the CHMP is subject to closer scrutiny.

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<sup>1</sup> Chapter 1, Section 3.3.

<sup>2</sup> Müller-Graff (2012), p. 27.

## 2.1 *Implementation of ICH guidelines in the EU: adoption through the EMA*

In the previous chapter, the five-step decision-making procedure leading to the adoption of ICH guidelines, culminating in the implementation of guidelines in the ICH regions, was analysed.<sup>3</sup> Thus, after the adoption of the ICH guideline on the global level (step 4), the regulatory parties are politically committed to implementing the guidelines into their regulatory framework (step 5). Although ICH guidelines are not legally binding on the global level, it was shown that the guidelines become de facto binding due to their epistemic legitimacy, and the political obligations following the largely consensus-based decision-making process.<sup>4</sup> The regional implementation takes place according to national or regional procedures applicable to the respective regulatory parties.<sup>5</sup> For example in the US, this entails the publication of a notice by the Food and Drug Administration (FDA) with the text of the ICH guideline in the Federal Register,<sup>6</sup> while in Japan, the guidelines will be published in English and Japanese on the website of the Pharmaceuticals and Medical Devices Agency (PDMA) together with an implementation date.<sup>7</sup>

In the EU, ICH guidelines are implemented through adoption by the Committee for Medicinal Products for Human Use (CHMP), thereby becoming EMA guidelines.<sup>8</sup> After adoption by the CHMP, these administrative guidelines are published on the website of the EMA, together with the other EMA soft law guidelines discussed in Chapter 3.<sup>9</sup>

The adoption of ICH guidelines through the CHMP, a Committee forming part of the EMA, rather than the Commission corresponds to the EU internal distinction between scientific as opposed to regulatory guidelines.<sup>10</sup> As the ICH guidelines are of a scientific nature defining quality, safety and efficacy criteria, they are implemented by the EMA. The EMA is responsible for the adoption of scientific guidance and specifically the CHMP, as the main scientific committee for human pharmaceutical products in the EU. The CHMP is well equipped for the adoption of these guidelines as it is the main organ forming an opinion on the authorisation of pharmaceuticals within the EMA, thus applying the guidelines on a day-to-day basis. Furthermore, the CHMP is involved already during the drafting process of the ICH guidelines, as the ICH topics form part of the work program of the CHMP's working parties and groups.<sup>11</sup> Also, the EU is generally represented by experts from the CHMP, and its working groups in the ICH Expert Working Groups that draft the ICH

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<sup>3</sup> Chapter 4, Section 4.1.

<sup>4</sup> Chapter 4, Section 6.2.

<sup>5</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 23.

<sup>6</sup> Lezotre (2014), p. 49. For more detail on the US implementation ICH guidelines see: J. Molzon, 'The Value and Benefit of the International Conference on Harmonisation (ICH) to Drug Regulatory Authorities: Advancing Harmonization for Better Public Health', in J. van der Laan & J. DeGeorge (Eds.), *Global Approaches in Safety Testing – ICH Guidelines explained* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. 23-28, p. 26f.

<sup>7</sup> Lezotre (2014), p. 49.

<sup>8</sup> L. Lindstrom 'ICH Guideline Implementation', in ICH, *The Value and Benefits of ICH to Drug Regulatory Authorities – Advancing Harmonization for Better Health* (2010), p. 9; Vamvakas (2013), p. 17.

<sup>9</sup> Chapter 3, Section 4.1.2.

<sup>10</sup> Chapter 3, Section 4.1.

<sup>11</sup> Lindstrom (2010), p. 9; Vamvakas (2013), p. 16. Also confirmed in an interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

guidelines.<sup>12</sup> In addition to the implementation of ICH guidelines, the European Medicines Agency has also published ‘Reflection Papers’ which aim at clarifying ICH guidelines.<sup>13</sup>

In general, the adoption of guidelines by the EMA follows a 10-step process, which has been applicable since 2005:

- Step 1 of drafting a guideline is the choice of a topic in the responsible scientific committee, working party or inspection group.
- In step 2 a rapporteur and in some cases a co-rapporteur are appointed by the respective body to be responsible for the respective topic.
- Step 3 consists of the drafting of a concept paper by the respective body, which will identify the matters that have to be addressed in the guideline without necessarily providing solutions. This concept paper will contain an ‘Impact Assessment’ anticipating the effects of the guideline on public health and also on the interested parties and involved regulatory authorities.
- The concept paper will then be adopted by the responsible scientific committee (step 4) and published on the EMA website for a two to three month-long public consultation, unless there is urgency in developing the guideline or it only concerns editorial changes to an existing guideline.
- Taking the received comments into account, the rapporteur then produces a draft guideline (step 5), which will be considered by the relevant working parties, the committees and the EMA secretariat. Should the relevant working party chairs, the EMA secretariat and the respective scientific committee chairs deem it necessary, it will be possible to additionally organise a meeting with interested parties.
- At the point where the draft guideline sufficiently represents the view of the members of the respective working party or other responsible group, the draft guideline is submitted to the appropriate organ indicated in the legal basis, which will adopt the draft guideline for a three to six month-long public consultation (step 6).
- Following the public consultation process, the designated working party or other group prepares a final version of the guideline (step 8), with consideration of the comments, and will submit it to the relevant scientific committee or other body for adoption.
- Step 9 then consists of the adoption of the guideline in the relevant scientific committee or other responsible body and its publication on the EMA website.
- Regarding the implementation (step 10), if the guideline does not include an implementation deadline, it will become operational six months after adoption.

According to the guideline adoption procedure communicated by the EMA, some of these EMA guidelines find their origin in existing legislative requirements, new technical and scientific developments, measures following on from international activities, or the

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<sup>12</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>13</sup> For example: EMA, Reflection paper on the requirements for selection and justification of starting materials for manufacture of chemical active substances, EMA/448443/2014, 16 September 2014.

cooperation with other regulatory authorities, or even on the proposal of interested parties.<sup>14</sup> The ICH and its counterpart for veterinary medicinal products, the VICH (International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products) are specifically mentioned as ‘international activities’ in the procedure document.<sup>15</sup> Thus, the EMA in this procedure document presents the ICH guidelines as ‘inspiration’ for the topic search in the adoption of CHMP guidelines.

However, it needs to be clarified that when they are adopted by the CHMP, the ICH guidelines do not follow the normal guideline adoption procedure with different drafting steps and public consultation, but are only endorsed. In the spirit of harmonisation this endorsement of course means that the guidelines are not to be changed in the implementation process. In essence, the 10-step guideline adoption procedure applicable to the EMA guidelines is replaced by the ICH five-step adoption procedure on the global level, which is then only followed by the formal adoption of the guidelines by the CHMP. The Rules of Procedure adopted by the ICH Assembly after the reform also stress that ‘to achieve true international harmonisation, it is important that ICH Guidelines are implemented consistently by all ICH Regulators’.<sup>16</sup> Therefore, ‘direct references’<sup>17</sup> are proposed as the preferred method for implementation and it is stressed that adding or omitting requirements defeats the harmonisation purpose of the guidelines.<sup>18</sup>

The EMA guidelines, and therefore also the implemented ICH guidelines, usually enter into force six months after their adoption.<sup>19</sup> Where the CHMP has adopted the ICH guidelines, the legal status is identical to the EMA guidelines, which do not originate in the ICH process.<sup>20</sup> They, therefore, can also be regarded as ‘quasi-binding’ and have the same practical as well as indirect legal effects on individuals, Member States and the EMA as adopting body as was identified for pharmaceutical guidelines in general in Chapter 3.<sup>21</sup> The implemented ICH guidelines even ‘replace existing guidelines on the subjects covered’.<sup>22</sup> The research for this thesis has shown that all guidelines adopted by the ICH have been implemented in the EU without fail. This flawless implementation record was also

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<sup>14</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 9f.

<sup>15</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 9.

<sup>16</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 4.

<sup>17</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 3.

<sup>18</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 5.

<sup>19</sup> Lindstrom (2010), p. 10; Vamvakas (2013), p. 17.

<sup>20</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 9.

<sup>21</sup> Chapter 3, Section 4.2.

<sup>22</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 9.

confirmed in interviews with the Commission and the EMA.<sup>23</sup> A list of all ICH guidelines including their corresponding EMA implementation guidelines is included in the Annex to this thesis.<sup>24</sup>

### 3. ICH GUIDELINES IN THE SOFT LAW GOVERNANCE OF PHARMACEUTICALS THROUGH THE EMA

Having discussed the implementation of the ICH guidelines through the European Medicines Agency, it remains to be evaluated which role the implemented guidelines play in the regulatory framework for pharmaceuticals in the European Union. It will be assessed how many ICH guidelines are adopted by the EMA, and how these ICH-originating guidelines relate to the guidelines developed solely within the agency. Moreover, cross-references to ICH guidelines in EMA originating guidelines will also be evaluated. In addition to that, the Common Technical Document (CTD), an ICH work product with significant influence on the pharmaceutical regulation in the EU, will be analysed.

#### *3.1 ICH guidelines in the administrative rule-making through the EMA*

In this regard, the analysis of the EU's pharmaceutical regulatory framework in Chapter 3 has shown that the European Medicines Agency is extensively involved in administrative rule-making through adopting guidelines.<sup>25</sup> In March 2015, of the 337 EMA scientific guidelines in force, 63 are implemented ICH guidelines adopted by the CHMP.<sup>26</sup> This amounts to a share of 19% of all scientific guidelines published by the EMA. Thus, roughly a fifth of the guidelines clarifying the legislative requirements of quality, safety and efficacy in the Union originate at the global level in the ICH.

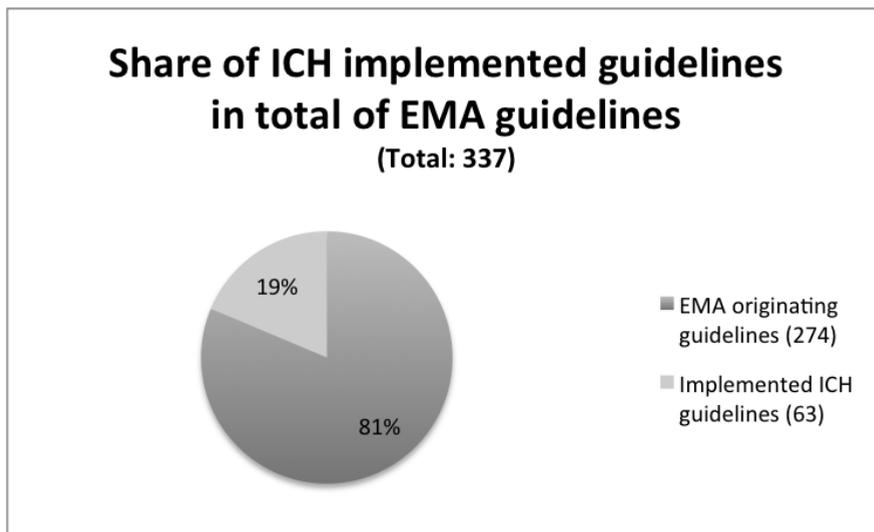
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<sup>23</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>24</sup> The list in the Annex reflects the status of ICH guidelines implemented in the EU as on 19 March 2015.

<sup>25</sup> Chapter 3, Section 4.1.2.

<sup>26</sup> The research reflects the status of guidelines as last updated on 19 March 2015.

**Figure 3: Share of ICH implemented guidelines in total of EMA guidelines**

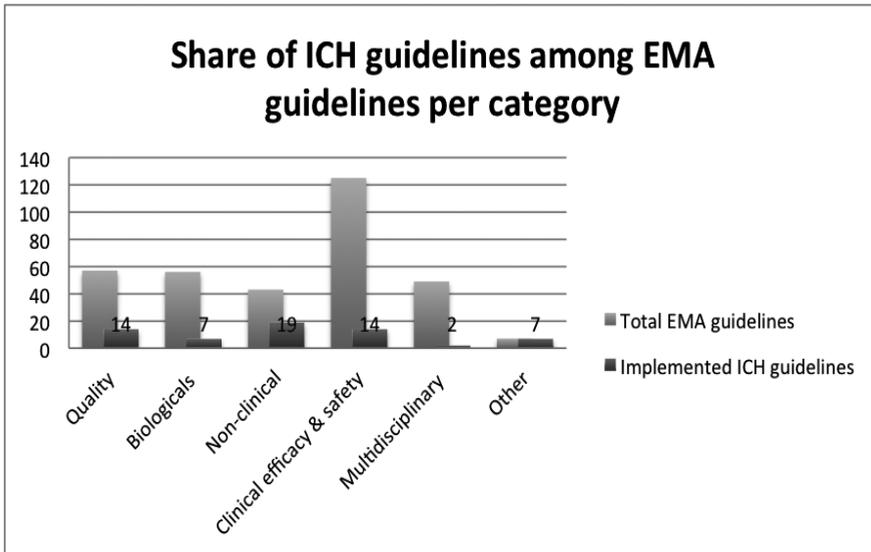
The influence of ICH guidelines is not evenly distributed throughout the categories of guidelines. In this regard, however, it needs to be mentioned that the guideline categorisation differs between the ICH and the EMA; while the ICH knows four categories of guidelines (quality, safety, efficacy and multidisciplinary),<sup>27</sup> the EMA operates a different categorisation (quality, biological, non-clinical, clinical efficacy and safety and multidisciplinary). Generally, the quota of ICH originating guidelines is higher in the categories of quality and safety than in the category of efficacy.<sup>28</sup>

In March 2015, 14 out of 57 EMA quality guidelines originated in the ICH.<sup>29</sup> In the area of biological medicines 7 out of 56 guidelines are implemented ICH guidelines, whereas in the area of non-clinical guidelines 19 out of 43 guidelines are implemented ICH guidelines. A low share of implemented ICH guidelines is to be found in the categories of clinical efficacy and safety, whereas out of 125 EMA guidelines only 14 originate in the ICH. In the category of multidisciplinary guidelines, only 2 of the 49 EMA guidelines are implemented ICH guidelines. However, 7 ICH originating guidelines are not included in any of the above categories on the EMA website. Thus, the influence of the ICH guidelines on European regulation is very much dependent on the category of guidelines concerned.

<sup>27</sup> Chapter 4, Section 6.1.

<sup>28</sup> Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>29</sup> The research, including the numbers in the following sentences, reflects the status of EMA guidelines as last updated on 19 March 2015.

**Figure 4: Share of ICH guidelines among EMA guidelines per category**

In this regard, it is important to mention that the ICH generally adopts guidelines, which are to be applied to all therapeutic classes of drugs.<sup>30</sup> The only exception to this approach is the E12 guideline for antihypertensive drugs.<sup>31</sup> In contrast to that, the EMA has adopted a multitude of guidelines tailored to specific therapeutic classes, namely classes of drugs categorised by the way they work or their chemical structure. Thus, in some areas, there might be an overarching ICH guideline supplemented by EMA guidelines applying to specific therapeutic classes of medicines.<sup>32</sup>

In order to understand the interaction between the guidelines originating in the EMA and the implemented ICH guidelines, this research also looked for references to ICH guidelines in the guidelines originating in EMA. In March 2015, out of the 274 guidelines originating in the EMA, 195 in some way refer or make reference to ICH guidelines. This means that 71% of the guidelines originating in the EMA include references to ICH guidelines. Therefore, the overarching majority of EMA originating guidelines does refer to ICH guidelines, either in a very general way or pointing to specific guidelines.

With regard to more general reference, a large number of EMA originating guidelines state that they should be read in conjunction with either ICH guidelines in general or specific ICH guidelines listed. Example 1 consists of a very general reference to other legal and soft

<sup>30</sup> Lezotre (2014), p. 52; Schneider (2003), p. 107.

<sup>31</sup> ICH, Draft ICH Consensus Principle – Principles for Clinical Evaluation of New Antihypertensive Drugs E12A, 2 March 2000. Due to the fact that the document sets principles which are accepted by ICH parties, but does not fully harmonise the topic due to remaining differences amongst the ICH regions, the ICH has classified E12A as a “Principle document” rather than a “Guideline”. However, for the purposes of this research, as the document is available on the guideline section of the ICH website, the document was counted as a guideline.

<sup>32</sup> Vamvakas (2013), p. 16. Vamvakas explains that for example in the area of clinical development, the ICH has established the general requirements, while the CHMP has adopted guidelines on the investigation of drugs in specific therapeutic fields such as cancer or diabetes.

law measures including ICH guidelines that should be read in conjunction with the respective EMA origination guideline. In example 2, the reference also provides that the EMA originating guidelines should be read in conjunction with legal and soft law measures including ICH guidelines, however, here the relevant ICH guidelines are specifically mentioned. Lastly, example 3 is a reference in the text of the guideline, which refers to a specific ICH guideline. All three types of references demonstrate that the EMA originating guidelines are also interrelated with the guidelines developed at the ICH level. Thus the scientific guidance of the EMA, whether originating in the agency itself or the ICH, has to be regarded as an integrated system of norms, with interrelated guidance documents.

**Example 1 (General Reference):**

‘This document should be read in conjunction with Directive 2001/83/EC (as amended) and all relevant CHMP and ICH Guidelines.’

From: Guideline on Carcinogenicity Evaluation of Medicinal Products for the Treatment of HIV Infection (EMA/CHMP/194898/2006)

**Example 2 (General reference but specifically identified ICH guidelines):**

‘This guideline has to be read in conjunction with the introduction and general principles of the Annex I to Directive 2001/83 as amended.

Pertinent elements outlined in current and future EU and ICH guidelines, should also be taken into account, especially those listed below:

- Dose-Response Information to Support Drug Registration (ICH E4)
- Statistical Principles for Clinical Trials (ICH E9)
- Choice of Control Group and Related Issues in Clinical Trials (ICHE10)
- Points to consider on an Application with
  - 1) Meta-analyses
  - 2) One pivotal study (CPMP/EWP/2330/99)
- Studies in Support of Special Populations: Geriatrics (ICH E7 CHMP/ICH/379/95) and related Q&A document (EMA/CHMP/ICH/604661/2009)
- Reflection paper on the extrapolation of results from clinical studies conducted outside the EU to the EU-population (EMA/CHMP/EWP/692702/2008)
- Note for guidance on antiarrhythmics (CPMP/EWP/237/95)
- Addendum to the Guideline on antiarrhythmics on atrial fibrillation and atrial flutter (EMA/CHMP/EWP/213056/2010).’

From: Guideline on clinical investigation of medicinal products for prevention of stroke and systemic embolic events in patients with non-valvular atrial fibrillation (EMA/CHMP/341363/2014).

**Example 3 (Text reference to specific ICH guidelines):**

‘When the cell substrate is obtained by recombinant DNA technology, a description of the expression system used for the production of antibodies should be in accordance with relevant guidelines, especially “Production and Quality Control of medicinal products derived by recombinant DNA technology”(3AB1A), and the relevant ICH guidelines Q5A (viral safety), Q5B (expression constructs) and Q5D (cell substrates).’

From: Guidelines on Development, Production, Characterisation and Specifications for Monoclonal Antibodies and Related Products (EMA/CHMP/BWP/157653/2007)

Moreover, there are also EMA originating guidelines which explicitly state that they were adopted due to a gap in ICH harmonisation. These are indicators of the fact that general ICH guidelines are often supplemented by EMA guidelines geared to specific cases. One example is to be found in the area of genotoxic impurities:

‘The toxicological assessment of genotoxic impurities and the determination of acceptable limits for such impurities in active substances is a difficult issue and not addressed in sufficient detail in the existing ICH Q3X guidances.’

From: Guideline on the limits of genotoxic impurities (EMA/CHMP/QWP/251344/2006)

Another example is to be found in the EMA guideline on impurities in antibiotics, which extensively explains the need to adopt a specific guideline for antibiotics although impurities are harmonised by the ICH:

‘Antibiotics active substances currently on the market are produced by fermentation, by fermentation followed by one or more synthetic steps (semi-synthetic substances) or by chemical synthesis. Fermentation processes are, in comparison to synthetic processes, more variable and less controllable, so the impurity profile of an active substance whose manufacturing process involves fermentation may be more complex and less predictable than that of a purely synthetic product. For this reason fermentation products and semi-synthetic substances are not included in the scope of the ICH Q3 and the VICH GL10/GL11 guidelines, which set thresholds for the identification, reporting and qualification of related impurities in active substances manufactured by chemical synthesis.

This guideline has been developed in order to provide guidance on how specifications for related impurities in antibiotics that are fermentation products or semi-synthetic substances derived from fermentation products, and are therefore not included in the scope of the (V)ICH guidelines mentioned above, should be set.’

From: Guideline on setting specifications for related impurities in antibiotics (EMA/CHMP/CVMP/QWP/199250/2009 corr)

To conclude, ICH guidelines account for a share of 19%, thus roughly a fifth of all EMA guidelines. Although this number is substantial, it does not accurately reflect the full impact of ICH guidelines in the EU. As the ICH guidelines cover harmonised rules for all medicinal products, these ICH guidelines often form the basis for further EMA guidelines for specific therapeutic classes. Moreover, as shown above, the EMA guidelines in 71% of cases contain references to ICH guidelines. Therefore, it can be concluded that the implemented ICH guidelines form an important part of the scientific guidance of the EMA, and the

implemented ICH guidelines together with the EMA originating guidelines form an integrated system of governance of pharmaceutical products through soft law measures.

### 3.2 *Common Technical Document (CTD)*

When assessing the impact of the ICH on European pharmaceutical regulation one major ICH work product must be mentioned specifically: the Common Technical Document (CTD), which establishes the format for the marketing authorisation application.

The impact of the CTD on European pharmaceutical regulation is significant, since it has streamlined the data requirements of all three regulatory authorities and has set one common standard format to which all the pharmaceutical companies have to adhere to. It has been qualified as possibly the ‘most significant new achievement of the ICH’<sup>33</sup> and even ‘one of the most ambitious and successful international harmonisation activities ever undertaken.’<sup>34</sup> In essence, the CTD (or its electronic version, the eCTD) has become the mandatory format for marketing authorisation applications in the EU and Japan. It became the highly recommended format for applications in the US, since the FDA’s Good Guidance Practices do not allow for ICH guidelines to become directly binding.<sup>35</sup> The CTD has also been adopted in Canada<sup>36</sup> and Switzerland.<sup>37</sup> Moreover, the CTD has been adopted or used as the basis for developing a marketing authorisation format in a multitude of other countries.<sup>38</sup> The acceptance of the CTD as a mandatory or highly recommended format is remarkable since it is a sign of the willingness to harmonise the information required for a marketing authorisation. Nonetheless, it should be pointed out that the first module of the CTD is still region-specific and contains administrative as well as prescribing information that is still diverging in the three regions.<sup>39</sup> Through the introduction of the CTD, the drafting of marketing authorisation applications had become less work-intensive for the applicants, as the laborious process of reformatting the application for every region can be omitted.<sup>40</sup>

The CTD was introduced in the EU in 2003. The CTD itself is established by four ICH guidelines. Whilst the ICH M4(R4) guideline is concerned with the organisation of information for marketing authorisation applications containing the overall structure of the CTD,<sup>41</sup> there are specific guidelines for the quality (M4Q(R1)),<sup>42</sup> safety (M4S(R2))<sup>43</sup> and

<sup>33</sup> Lee (2005), p. 180.

<sup>34</sup> J. Molzon, ‘The International Conference on Harmonization Common Technical Document – Global Submission Format’, 60(3) *Food and Drug Law Journal* (2005), pp. 447-451, p. 450.

<sup>35</sup> Molzon (2005), p. 449. For the European Union see: Annex1 of Directive 2001/83/EC specifically in preamble paras. (2) and (3).

<sup>36</sup> <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/ctd/index-eng.php>, last accessed: 3 April 2017.

<sup>37</sup> <https://www.swissmedic.ch/zulassungen/00153/00189/00197/01370/index.html?lang=de>, last accessed: 3 April 2017.

<sup>38</sup> Y. Juliet, ‘CTD – A Tool for Global Development and Assessment’, 3(2) *Drug Information Association Global Forum* (2011), pp. 25-26, p. 26; Lezotre (2014), p. 58.

<sup>39</sup> Molzon (2005), p. 449.

<sup>40</sup> ICH, *The Value and Benefits of ICH to Drug Regulatory Authorities – Advancing Harmonization for Better Health* (2010), p. 2.

<sup>41</sup> ICH, ICH Tripartite Guideline – Organisation Of The Common Technical Document For The Registration Of Pharmaceuticals For Human Use M4, 5 June 2016.

<sup>42</sup> ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Quality – M4Q(R1) – Quality Overall Summary Of Module 2 And Module 3: Quality, 12 September 2002.

efficacy (M4E(R1))<sup>44</sup> sections of the CTD. These four guidelines have also been adopted by the EMA, like any other ICH guidelines.<sup>45</sup> However, since the mandatory format for the marketing authorisation in the EU was contained in Annex 1 of Directive 2001/83/EC this Annex had to be amended. In this regard, Article 120 of Directive 2001/83/EC delegates the competence for amendments to Annex 1 to the European Commission, which can carry out amendments through a comitology procedure. The Commission then through Commission Directive 2003/63/EC introduced a new Annex 1 to Directive 2001/83/EC, implementing the CTD.<sup>46</sup> Moreover, the Commission adopted Volume 2B of the Notice to Applicants 'Presentation and content of the dossier'.<sup>47</sup>

The CTD consists of five modules. The first one contains administrative information being addressed to the respective regulatory authority where the marketing authorisation is applied for example with regard to labelling. The other four modules contain an overall introduction and summary as well as data concerning the quality of the product, nonclinical study reports and clinical study reports.<sup>48</sup>

In essence, the CTD serves as guidance for which ICH guidelines apply to the corresponding part of the marketing authorisation. While ICH guidelines have harmonised a wide field of requirements for the registration of medicinal products, what the CTD does is to put them into order in one consistent document, forming the dossier that companies have to submit to obtain marketing authorisation. Within the different modules of the CTD reference is made to the ICH guidelines that are applicable, as the following excerpt from the Quality Module shows:

3.2.S.3.1 Elucidation of Structure and other Characteristics (name, manufacturer)

NCE:

Confirmation of structure based on e.g., synthetic route and spectral analyses should be provided. Information such as the potential for isomerism, the identification of stereochemistry, or the potential for forming polymorphs should also be included.

Reference ICH Guideline: Q6A

Biotech:

For desired product and product-related substances, details should be provided on primary, secondary and higher-order structure, post-translational forms (e.g., glycoforms), biological activity, purity, and immunochemical properties, when relevant.

Reference ICH Guideline: Q6B

<sup>43</sup> ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Safety – M4S(R2) – Overview And Nonclinical Summaries Of Module 2 – Organisation Of Module 4, 20 December 2002.

<sup>44</sup> ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Efficacy – M4E(R2) – Overview And Clinical Summary Of Module 2- Module 5 Clinical Study Reports, 15 June 2016.

<sup>45</sup> See the list of implemented ICH guidelines in the Annex.

<sup>46</sup> Commission Directive 2003/63/EC of 25 June 2003 amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use, OJ L 159, 25 June 2003, pp. 46-94.

<sup>47</sup> On the Notice to Applicant see Chapter 3, Section 4.1.1.

<sup>48</sup> Molzon (2005), p. 449.

## 3.2.S.3.2 Impurities (name, manufacturer)

Information on impurities should be provided.

Reference ICH Guidelines: Q3A, Q3C, Q5C, Q6A, and Q6B

From: Common Technical Document for the Registration of Pharmaceuticals for Human Use Quality Overall Summary of Module 2 and Module 3: Quality (CPMP/ICH/2887/99 – Quality)

Furthermore, the CTD facilitates the exchange of information amongst regulatory authorities.<sup>49</sup> However, this format should not only be seen as a formal requirement, but indeed has an influence on the way the review of marketing authorisations is exercised.<sup>50</sup> The development of the CTD was complicated by the fact that the harmonisation of the format also required looking into the content of the marketing authorisation applications, to ensure that the terms used had the same meaning in the regions.<sup>51</sup> Thus, with the CTD the ICH developed a ‘common regulatory language’.<sup>52</sup> Moreover, putting the information submitted by the applicant into a specific order shapes the review process and makes it more efficient.<sup>53</sup>

Ultimately, Lee sees the common format as a possible step towards mutual recognition of marketing authorisations.<sup>54</sup> Indeed, when comparing the development of the CTD to the history of pharmaceutical regulation in the EU,<sup>55</sup> similarities become apparent. In the history of EU integration, the harmonisation of the marketing authorisation application provided a basis for the mutual acceptance of marketing authorisations, as well as for the scientific data required in order to demonstrate the quality, safety and efficacy of a medicinal product. However, in the interviews conducted for this research with officials of the EFPIA<sup>56</sup> and the Commission<sup>57</sup> as well as the EMA,<sup>58</sup> the officials do see obstacles to mutual recognition of marketing authorisation between the ICH regions; it does not seem to be politically possible yet due to the loss of sovereignty connected to such a development. Moreover, it might allegedly require substantial changes in the legislative framework.<sup>59</sup> Although a mutual

<sup>49</sup> Molzon, Giaquinto, Lindstrom, Tominaga, Ward, Doerr, Hunt & Rago (2011), p. 504. This was also confirmed in an interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>50</sup> Molzon, Giaquinto, Lindstrom, Tominaga, Ward, Doerr, Hunt & Rago (2011), p. 507; Juliet (2011), p. 25.

<sup>51</sup> Juliet (2011), p. 25.

<sup>52</sup> Kuhnert (2011), p. 18.

<sup>53</sup> Molzon (2013), p. 26.

<sup>54</sup> Lee (2005), p. 181. See also: K. Purnhagen, ‘The Challenge of Globalization in Pharmaceutical Law – Is an International Drug Approval System Modeled after the European System Worth Considering?’, 63(3) *Food and Drug Law Journal* (2008), pp. 623-645. Purnhagen discusses the possibility of establishing a system based on the European decentralized procedure on the global level.

<sup>55</sup> Chapter 3, Section 2.

<sup>56</sup> Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>57</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>58</sup> Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>59</sup> This point was especially raised in the interviews with the EMA officials as well as the EMA’s Legal Department. Interview with two officials of the Legal Department of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author;

recognition of marketing authorisations between the ICH parties is not currently planned, the CTD has certainly contributed to the feasibility of future developments into this direction.

#### 4. INFLUENCE OF ICH GUIDELINES ON LEGISLATION, ADMINISTRATIVE RULE-MAKING AND THE JUDICIARY

As the previous sections have shown the implementation of ICH guidelines takes place through the adoption of administrative soft law measures in the form of EMA guidelines, which form an important part of the EMA scientific guidance. This section will examine the influence of the ICH guidelines beyond the EMA. Indeed, ICH guidelines have an impact on other acts like Commission guidelines, and even legislative measures, as the following analysis will demonstrate. Moreover, it is scrutinized whether ICH guidelines might also have an influence on the judiciary, looking at the use of ICH guidelines in the Court of Justice.

##### 4.1 *ICH influence on Commission guidelines*

In Chapter 3 an analysis was carried out to show that not only does the EMA adopt guidance measures, but that the Commission has published an extensive soft law framework for the governance of medicinal products in the form of regulatory guidelines.<sup>60</sup> These Commission guidelines, compiled in the ‘The rules governing medicinal products in the European Union’, can be influenced by ICH harmonisation.

First of all, the Commission guidelines make references to CHMP guidelines implementing ICH guidelines in some instances. This can be seen in the field of clinical trials, where the CT-3 guideline states that this guidance ‘is to be read in conjunction with, in particular: (...) the Note for guidance on clinical safety data management: Definition and standards for expedited reporting (‘note for guidance ICH E2A’).<sup>61</sup> In a footnote to this provision, reference is made to the CPMP/ICH/377/95.

Moreover, at least in one instance there is evidence that a Commission guideline has been changed on the basis of an ICH guideline. In the regulation of the Good Manufacturing Practice (GMP), in addition to binding legislative measures, the Commission adopted the EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, which are compiled in Volume 4 of the Rules Governing Medicinal Products in the EU. Chapter 1 of Volume 4 deals with the Pharmaceutical Quality System. On the cover page it is stated that amendments to this chapter have been made according to the ICH Q10 guideline, leading also to a change in the title of the Chapter.<sup>62</sup> Thus, the ICH guidelines evidently also influence the European Commission guidelines in the EU framework of pharmaceutical regulation.

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interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>60</sup> Chapter 3, Section 4.1.1.

<sup>61</sup> European Commission, Communication from the Commission – Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use (‘CT-3’), (2011/C 172/01), 1.4 (9).

<sup>62</sup> European Commission, EudraLex, The Rules Governing Medicinal Products in the European Union Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use Chapter 1 Pharmaceutical Quality System, SANCO/AM/sl/ddg1.d.6(2012)860362, p. 1.

#### 4.2 ICH influence on EU pharmaceutical legislation

Apart from the implementation of ICH guidelines through the CHMP in the form of soft law administrative guidelines, ICH harmonisation can also have an impact on legislation.<sup>63</sup> This is remarkable as the EU's core pharmaceutical legislation, laid down in Directive 2001/83/EC and Regulation (EC) 726/2004, does not share the same obligation to take international standards into account in the drafting of legislation concerning medicinal products, as can be found for example in the General Food Law.<sup>64</sup>

The ICH Q7 guideline on Good Manufacturing Practice (GMP) is exemplary for showing the influence of ICH standards on legislation.<sup>65</sup> Directive 2001/83 had to be amended in the aftermath of the agreement at the ICH on the Good Manufacturing Practice, which not only regulates the good manufacturing practice for the finished medicinal product, but also applies to the starting materials used. Through Directive 2004/27<sup>66</sup> the requirements of the good manufacturing practice were also extended to starting materials for pharmaceutical product in Article 46(f) of Directive 2001/83. Moreover, it added paragraphs to Article 47 of the Directive, based on which the Commission then was delegated the power to adopt a renewed GMP guideline, as Volume 4 of 'The Rules Governing Medicinal Products in the European Union'.<sup>67</sup> This Commission GMP guideline then implemented the ICH Q7 guideline. Thus, ICH Q7 broadened the scope of the good manufacturing practice legislation in the European Union and, additionally, led to the adoption of a new soft law measure by the Commission.

The ICH E6 guideline on Good Clinical Practice was also very influential on the regulation on clinical trials in the EU. In this case, the E6 guideline influenced Directive 2001/20/EC regulating clinical trials in Europe, that was adopted after the ICH E6 guideline was agreed upon.<sup>68</sup> It largely takes over the definitions and general principles established in the ICH guideline, often even literally, and then creates an institutional framework and procedure applicable in the EU to structure clinical trials accordingly. Furthermore, the same is true for the Good Clinical Practice Commission Directive 2005/28/EC,<sup>69</sup> which reflects on provisions from the ICH E6 guideline on general good clinical practice principles in Section 1. The Commission Directive then continues with the establishment of a European procedure for the authorisation of the manufacturing or import of the medicine to be investigated in a clinical trial, as well as procedures for the inspection of clinical trials. So the influence of ICH guidelines in the regulation of clinical trials runs as a common thread through the overall legal framework for clinical trials.

It should be mentioned that the framework for clinical trials has been revised due to

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<sup>63</sup> Molzon, Giaquinto, Lindstrom, Tominaga, Ward, Doerr, Hunt & Rago (2011), p. 508; Vamvakas (2013), p. 16.

<sup>64</sup> See Chapter 1, Section 3.3.

<sup>65</sup> Lindstrom (2010), p. 10.

<sup>66</sup> Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 136, 30 April 2004, pp. 34-57.

<sup>67</sup> Directive 2001/83/EC, (OJ L 311, 28 November 2001, pp. 67-128), Art. 47.

<sup>68</sup> Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, OJ L 121, 1 May 2001, pp. 34-44.

<sup>69</sup> Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products, OJ L 91, 9 April 2005, pp. 13-19.

criticism that it led to a decrease of clinical trials in Europe, that it was too strict for non-commercial clinical trials (for example carried out in universities), and furthermore, due to increasing calls for transparency with regard to clinical trials data.<sup>70</sup> It is difficult to assess whether these problems originate in the ICH or the EU implementation without expert knowledge. The new Regulation 536/2014 is far more detailed than Directive 2001/20/EC, which complicates tracing ICH generated norms in the Regulation.<sup>71</sup> In the new clinical trials Regulation the EU seems to have emancipated itself from the literal transposition of ICH definitions. As it is a Regulation, the procedures for the Member States are described very much in detail, which is contrary to the general practice in pharmaceutical regulation of leaving scientific details to be determined in guidelines. Thus, whereas the Regulation is concerned with the coordination of the respective procedures, the ICH E6 is more concerned with the actual running of the clinical trial. However, in the Preamble of the Regulation the ICH and its clinical trial guidelines are referred to in the sense that they should 'be taken appropriately into account for the application of the rules set out in this Regulation, provided that there is no other specific guidance issued by the Commission and that those guidelines are compatible with this Regulation.'<sup>72</sup> Therefore, although the influence of the ICH on the clinical trials legislation might have faded, its effect on the EU's technical and scientific guidelines still seems to persist.

Conclusively, the impact of ICH guidelines in the EU's regulatory framework for pharmaceuticals in some cases extends beyond the soft law implementation via the EMA, to an influence on the Commission's pharmaceutical guidelines and even legislative provisions. This finding is important as it shows that, beyond implementation through EMA guidelines, the effects of the ICH shape pharmaceutical legislation in the EU even where this is less visible and might require careful comparison of the texts in order to be detected.

### 4.3 ICH standards and the Court of Justice: Implemented ICH guidelines used in Court

The previous sections of this chapter have demonstrated the extensive influence of ICH standards on pharmaceutical regulation in the EU with regard to hard and soft law. However, the influence of global standards in some instances extends beyond the administrative and legislative regulation to the judiciary,<sup>73</sup> where global standards are used in court, as is exemplified in the area of foodstuffs through the extensive use of Codex Alimentarius standards through the Court of Justice.<sup>74</sup>

<sup>70</sup> See: Euractiv, 'Brussels seeks to simplify rules on clinical trials', 18 July 2012, available via: <http://www.euractiv.com/health/brussels-vows-simplify-clinical-news-513975>, last accessed: 3 April 2017; Euractiv, 'MEP's give resounding 'yes' to new clinical trials rules', 30 Mai 2013, available via: <http://www.euractiv.com/health/meps-clinical-trials-need-clear-news-528127>, last accessed: 3 April 2017.

<sup>71</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, OJ L 158, 27 May 2014, pp. 1-76. See: M. Rizzi, 'Simple, Safe And Transparent (?): Preliminary Reflections on the Proposal for a New EU Regulation of Clinical Trials', 4(4) *European Journal of Risk Regulation* (2013), pp. 534-538.

<sup>72</sup> Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, OJ L 158, 27 May 2014, pp. 1-76, Preamble (43).

<sup>73</sup> See also: Müller-Graff (2012), p. 29.

<sup>74</sup> For example, in the *Beer Purity* case (Case 178/84 *Commission v. Germany*, ECLI:EU:C:1987:126), the Court made clear that in judging whether a restriction to the free movement of goods is justified under the public health exemption, it takes into account 'international scientific research', specifically mentioning the Codex. In the area of food safety, it is a well-established

With regard to pharmaceuticals, such a practice of references of the Court to ICH standards has not developed until now. A search of the Court's curia database does not reveal any instances of the Court relying on ICH standards in its case law.<sup>75</sup> Nonetheless, in two Court orders related to the access of documents in clinical trials data, the ICH is mentioned. However, the Court only reproduces a statement of the EMA: that scientific guidelines governing clinical trials are published also by the ICH.<sup>76</sup> This statement has not been subject to further discussion in the order and remains merely additional information.

However, it needs to be taken into account that depending on how the standard is implemented in the EU, the Court could use global standards either directly or indirectly. Whereas the direct use of standards would entail that the Court makes reference to the global standard as such, indirect references in this regard are cases where the Court relies on EU soft or hard law measure implementing a global standard. With indirect references, it is difficult to recognise whether the Court is actually relying on a global standard. It must first be known that the European measure the Court is using as an interpretative tool actually originates in a global standard. For ICH standards, their implementation takes place through EMA guidelines, thus administrative soft law measures. Therefore, it is worthwhile to look into the case law on pharmaceuticals in the EU and to assess whether the Court is using soft law measures as an interpretative aid in its case law. In the area of pharmaceutical regulation,

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practice that the Court uses Codex standards as interpretative aid. (See: Masson-Matthee (2007), p. 103ff). The Court also used the Codex to assess national administrative measures such as the classification of foodstuffs, as exemplified by the *Sachsenmilch* case surrounding the question of classification of mozzarella cheese. (Case 196/05 *Sachsenmilch v. Oberfinanzdirektion Nürnberg*, ECLI:EU:C:2006:383, para. 29.) The Court has used the Codex standards to assess the justification of administrative decisions of the Union as well as the previously mentioned decisions of Member State bodies. (See also: Pereira (2010), p. 556f.) In a preliminary ruling on the highly debated area of the regulation of genetically modified organisms (GMOs), the Court in the *Monsanto* case made a reference to the Codex Alimentarius to clarify the concept of 'substantial equivalence' in the novel food regulation. (C-236/01 *Monsanto Agricoltura Italia SpA and Others and Presidenza del Consiglio dei Ministri and others*, ECLI:EU:C:2003:431, para. 79.)

<sup>75</sup> Search of the official CJEU website (<http://curia.europa.eu>), for text references to "ICH" or "International Conference on Harmonisation" and "International Council for Harmonisation", last verified on 24 April 2016.

<sup>76</sup> Order of the President of the General Court of 25 April 2013 in case T-44/13 R *AbbVie v. EMA*, ECLI:EU:T:2013:221, para. 66; Order of the President of the General Court of 25 April 2013 in case T-73/13 R *InterMune UK and Others v. EMA*, ECLI:EU:T:2013:222, para. 52. Paragraph 52 of the *InterMune* Order states: 'Consequently, there is no case law enabling an answer to be given easily to the question on which judgment will have to be delivered subsequently on the substance, that is to say, whether the contested decision, based on the EMA's new disclosure policy, infringes the applicants' right to professional secrecy, as guaranteed by Article 339 TFEU and Article 7 of the Charter, on the grounds that the information at issue is confidential in nature and must therefore be protected against any disclosure (see paragraph 31 above). This involves a question of principle affecting the functioning of the pharmaceuticals and biotechnology sector in Europe and worldwide. The EMA points out that one of its principal roles consists in generating information for the public on the conduct of the various clinical and non-clinical trials necessary for obtaining an MA. The EMA adds that scientific guidelines on clinical trials, including clinical safety and clinical study reports, are also published following agreement on a harmonised approach between Europe, Japan and the United States of America by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. The EMA further states that it provides guidelines for non-clinical trials of medicinal products, intended for pharmacology, pharmacokinetics and toxicology.' The *AbbVie* paragraph is worded similar.

one of the best-known cases in which the Court used non-binding measures to rule on a dispute is the *Chemische Fabrik Kreussler* case, which dealt with the distinction between cosmetic and medicinal products.<sup>77</sup> The Court affirmed that a guidance document, which was drafted by the Commission together with the Member States on the distinction in question, can be taken into account by national courts, and was in fact relied upon by the Court itself in the case.<sup>78</sup> According to the Court the guidance document, although not legally binding, ‘may provide useful information for the interpretation of the relevant provisions of European Union law and therefore contribute to ensuring that they are applied uniformly’.<sup>79</sup> There are several other instances in which the Court relied on Commission or agency guidelines in order to interpret the law applicable to disputes it was called to adjudicate.

A very prominent role was played by an EMA note for guidance in the *Artegodan* case, dealing with the withdrawal of marketing authorisations by the Commission.<sup>80</sup> The Commission decision was based on an assessment of the EMA, which in turn relied on a CPMP note for guidance. This guideline, adopted after the products had been authorised, introduced a change in the evaluation criteria for the benefit/risk assessment of medicines treating obesity,<sup>81</sup> stating that ‘(t)herapeutic efficacy for treating obesity requires a significant and long-term lowering of body weight (of at least one year)’.<sup>82</sup> This change in scientific evaluation of the efficacy of such products led to a withdrawal of their marketing authorisations, since the benefit/risk assessment based on this new criterion was considered negative for the concerned products.<sup>83</sup> The Court in *Artegodan* goes into detail in assessing whether the guideline indeed changes the evaluation criteria and whether this change is based on new scientific data, which would justify the withdrawal of a marketing authorisation.<sup>84</sup> It came to the conclusion that it did not establish a new criterion for

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<sup>77</sup> Case C-308/11 *Chemische Fabrik Kreussler v. Sunstar Deutschland*, ECLI:EU:C:2012:548. In this case the guideline subject to discussion was not one of the Eudralex Commission regulatory guidelines discussed in Chapter 3, but a Guideline by DG Enterprise and Industry regulating medical devices.

<sup>78</sup> Case C-308/11 *Chemische Fabrik Kreussler v. Sunstar Deutschland*, ECLI:EU:C:2012:548, paras. 25-27 and 29. See also: T. Ehnert, *Regulating the Invisible – A Critical Analysis of the EU’s Approach to Nanotechnologies* (Maastricht: Universitaire Pers Maastricht, 2015), p. 62.

<sup>79</sup> Case C-308/11 *Chemische Fabrik Kreussler v. Sunstar Deutschland*, ECLI:EU:C:2012:548, para. 25. The Court in this paragraph reaffirms the introduction of the respective guideline.

<sup>80</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283. The note for guidance in question was the CPMP Note for Guidance on clinical investigation of drugs used in weight control (CPMP/EWP/281/96).

<sup>81</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, paras. 162 and 164.

<sup>82</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, para. 39.

<sup>83</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, paras. 203 and 209.

<sup>84</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, paras. 211-216.

assessing the efficacy of the medicinal products in question.<sup>85</sup> The Court also concluded that a mere change in the scientific evaluation, without new scientific data, does not justify a withdrawal.<sup>86</sup> Thus, in this case the assessment of the guideline led the Court to finding a breach of EU law with regard to the Commission Decisions, leading to their annulment.<sup>87</sup>

Also in the *Novartis* case, a preliminary ruling concerning the UK marketing authorisation of generic medicinal products – medicines that are equivalent to authorised products – the Court referred back to the ‘Notice to Applicants’ to define which cases the generic authorisation procedure could be used in.<sup>88</sup> Moreover, there was the *Nycomed* case, where permission was denied to omit the otherwise mandatory submission of a paediatric investigation plan, a so-called waiver. Here, the applicant Nycomed Danmark ApS relied amongst others on a Commission guideline.<sup>89</sup> Nycomed referred to a guideline to support its argument concerning the interpretation of concept of ‘disease or condition for which the medicinal product is intended’.<sup>90</sup> The Court subsequently used the same guideline to prove the applicant’s interpretation wrong.<sup>91</sup> The guideline used in the case does contain references to the ICH E11 guideline, however, this is only for the purpose of defining the age classification in the paediatric population, and not with regard to the disputed concept.<sup>92</sup>

In none of the above-mentioned cases apart from the *Nycomed* case were the guidelines relied upon by the Court implemented ICH guidelines, and nor did they contain ICH references. While in the *Nycomed* case the guideline did contain ICH references these were not disputed in court. Thus, for now, there is no case where an indirect reliance on ICH standards by the Court can be proven. However, the possibility of indirect reliance exists. As established before, European soft law governing pharmaceuticals is heavily influenced by the ICH standards, and the Court relies on this soft law in the form of Commission and EMA

<sup>85</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artogodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, para. 212.

<sup>86</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artogodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, para. 211.

<sup>87</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artogodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, paras. 220 and 221.

<sup>88</sup> Case C-106/01 *Novartis Pharmaceuticals UK Ltd v. The Licensing Authority established by the Medicines Act 1968*, ECLI:EU:C:2004:245, para. 53.

<sup>89</sup> Case T-52/09 *Nycomed Danmark v. EMA*, ECLI:EU:C:2011:83. The guideline in question was: European Commission, Commission Communication – Guideline on the format and content of applications of agreement or modification of a paediatric investigation plan and request for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies (OJ C 243, 24 September 2008), pp. 1-12.

<sup>90</sup> Case T-52/09 *Nycomed Danmark v. EMA*, ECLI:EU:C:2011:83, para. 78. The disputed concept is to be found in Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (OJ L378, 27 December 2006), pp. 1-19, Art. 11(1)(b).

<sup>91</sup> Case T-52/09 *Nycomed Danmark v. EMA*, ECLI:EU:C:2011:83, para. 79.

<sup>92</sup> European Commission, Commission Communication – Guideline on the format and content of applications of agreement or modification of a paediatric investigation plan and request for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies, OJ C 243, 24 September 2008, pp. 1-12, point 2.1, 2.5.1.2, 2.5.5.1 and 2.5.5.4. In these points the guideline refers to the ICH E 11 guideline with regard to the age group classification contained in the guideline and the timing of the measures.

guidelines in order to judge disputes. Where the guidelines would be implemented ICH guidelines or where they contain ICH references, this could amount to the use of ICH guidelines through the Court. Such a direct or indirect reference to an ICH guideline through the Court would then certainly ‘amplify’ the legal effects of the originally non-binding norm.

## 5. CONCLUSION

This chapter has established that global standards require a connecting measure in order to be incorporated into the EU regulatory framework. In contrast to international agreements they have to be implemented in the EU regulatory framework either through different variations of legislative implementation, or through the incorporation of administrative soft law measures. With regard to the standards developed by the ICH, the implementation takes place through adoption of the ICH guidelines by the EMA. Within the EMA’s scientific guidance, these implemented ICH standards account for about a fifth of the total guidelines adopted by the agency. The share of ICH measures in EMA guidelines varies according to the category of guidelines concerned.

However, it is difficult to truly separate between ICH originating guidelines and the guidelines originating in the EMA, as together they form an integrated governance system with interconnected guidelines. Whereas the ICH guidelines apply to all therapeutic classes, the EMA has adopted a multitude of guidelines for specific therapeutic classes, such as specific rules for medicines treating a certain illness, or groups of medicines working in a specific way. The large majority of the EMA originating guidelines make references to ICH guidelines and should be applied together with these. Moreover, alongside the individual guidelines, the ICH has shaped the format of marketing authorisation applications through the introduction of the CTD. Apart from relieving the marketing authorisation applicants from the re-drafting of the application for every region, the CTD has also improved the exchange of information between the regulatory authorities.

Moreover, it was shown that beyond the implementation of the ICH guidelines as EMA guidelines, the standards set on the global level also have an effect on European pharmaceutical legislation and the soft law measures established by the European Commission. In the regulation of the Good Manufacturing Practice and the Good Clinical Practice, the adoption of ICH guidelines has led to the broadening of the scope of legislation, and some legislative acts contain (often literal) transpositions of ICH norms. Moreover, it has been shown that ICH guidelines are referenced to in Commission guidelines and that such regulatory guidelines have been amended to conform to ICH standards. In addition to these effects on the legislative and administrative rules applying to pharmaceuticals in the EU, it was also argued that global standards are used as an interpretative aid in front of the Court, either directly or indirectly. While for the pharmaceutical standards developed by the ICH such a practice cannot currently be proven, it was shown that soft law measures are relied upon by the Court in the interpretation of pharmaceutical law and, therefore, the potential route to (the indirect) use of global pharmaceutical standards in EU case law is open.

Overall, this chapter has established that although the guidelines developed by the ICH are to be qualified as soft law, in practice they are implemented without fail as EMA guidelines in the European Union. They substantially shape the regulation of pharmaceuticals on the agency level and also affect Commission soft law and even legislation. Furthermore, they can serve as an interpretative aid in front of the Court. Thus, when looking beneath their soft law ‘cover’, these standards are powerful tools in the regulation of pharmaceuticals. Their extensive effect on European pharmaceuticals regulation raises questions of legitimacy, which will be analysed in the following chapter.



## Chapter 6: Examining the legitimacy of the ICH standard-setting procedure and uploading EU administrative law

### 1. INTRODUCTION

The previous chapters have shown that global standard-setting as an emerging phenomenon gives rise to several legal challenges. The shift from government to (global) governance with new forms of global regulatory cooperation as well as the increasing role of private parties in standard-setting and reliance on soft law mechanism, are deviating from the traditional model of command-and-control state regulation of risk. This creates challenges in terms of the legitimacy of these regulatory standards set on the global level.

In the area of pharmaceutical regulation, Chapter 5 on the implementation of ICH standards in the EU revealed that ICH standards are implemented into the EU's pharmaceutical regulatory framework through the EMA. They also influence legislation as well as Commission guidelines, and have the potential to be used as an interpretative tool by the Court. It has been shown that these standards are reliably implemented in the EU and form an integral part of the regulatory framework. This raises questions regarding the legitimacy of the ICH standards.

In the search of a framework for assessment of the legitimacy of global-standard setting bodies, Chapter 2 proposed the evaluation against procedural norms developed by EU administrative law. Following this argument, it is imperative to examine whether the procedure through which the ICH standards are adopted lives up to the administrative law principles, that similar measures originating in the EU itself have to fulfil. In this respect, the administrative and good governance principles of participatory openness, transparency, and independent expertise have been identified as core benchmarks in examining the standard-setting procedure.

In order to apply a European perspective on questions of participation, transparency, and independence of experts it, first of all, needs to be acknowledged that these principles do not have a fixed definition or tangible requirements that have to be fulfilled. Even if participation (Article 10(3) and 11 TEU), transparency (Articles 10(3) and 11 TEU, Article 15 TFEU), and independent expertise (Article 298(1) TFEU, 'open efficient and independent European administration') are principles enshrined in the Treaties, their content is not clarified in detail. Most administrative procedures are regulated in a policy-specific way, through legislation and also through rules of procedure set by the individual bodies themselves. This means that although the same procedural principles apply to European institutions and bodies, the substantive requirements of these principles are not coherently regulated in detail.<sup>1</sup> This leads to a 'patchwork blanket'<sup>2</sup> of procedural rules applicable to administrative action in the EU. Therefore, in this chapter, when applying a European perspective to participation, transparency and independent expertise in the ICH process, there will be a specific assessment of what procedural standards are applicable in the guideline development process of the European Medicines Agency, by analogy. This analogy is based on the fact that the ICH standards implemented in the EU in the form of EMA guidelines and also the EU-originating scientific guidelines – which would be comparable to ICH guidelines – are adopted by the EMA.

This chapter will not only compare the procedural standards applicable and identify potential legitimacy gaps in the ICH procedure, when compared to the EMA procedure, but

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<sup>1</sup> Chapter 2, Section 5.2.

<sup>2</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 67.

it will also provide recommendations for policies and practices that can be ‘uploaded’ from the EMA standard-setting procedure to the ICH level.<sup>3</sup> Thus, while assessing the ICH process from the perspective of EU administrative law as the EU is implementing the ICH standards, the chapter also aims at providing inspiration for the ICH process on the global level as such. Moreover, from a broader perspective, the ‘uploading’ of the EMA procedural standards for the adoption of pharmaceutical standards also allows for suggestions on how procedural standards of a Global Administrative Law could develop. As pointed out in Chapter 2, currently scholars of Global Administrative Law and International Administrative Law are in the process of identifying and developing a legal framework for regulatory cooperation on a global level. The identification of policies and practices that can be ‘uploaded’ from the European level to the global level – even within a specific case study, such as pharmaceuticals – can contribute to developing procedural standards for a prospective Global Administrative Law.

The chapter therefore simultaneously addresses legitimacy concerns from different perspectives. On the one hand, the EU as an implementing regulatory system should be concerned about the legitimacy of pharmaceutical standards set on the global level as they become an integral part of the EU regulatory framework. On the other hand, where the procedural policies and practices applied in the EU are ‘uploaded’ to the ICH, it might contribute to the ICH as a body on the global level being able to address legitimacy challenges arising from an emerging Global Administrative Law. In this regard, it will focus on the procedural principles of participation (Section 2), independent expertise (Section 3), and transparency (Section 4).

## 2. PARTICIPATION

Beyond the state level most bodies will not be able to rely on democratic legitimacy through elections.<sup>4</sup> Therefore, they have to rely on a ‘surrogate political process’, meaning that since they are not electorally legitimised they rely on other means to increase their legitimacy, such as inclusive participation of all relevant stakeholders.<sup>5</sup> Nevertheless, the influence that can be exerted through participation is subject to limitations as ‘it is the right to be heard, not the right to decide’.<sup>6</sup> However, along with a potential contribution to legitimacy, the participation of stakeholders in the decision-making process serves the accountability of the decision-makers as well as the quality of the decision taken. This is due to the contributions stakeholders make to the process.<sup>7</sup>

As for many administrative law and good governance principles a fixed, universally applicable definition is also lacking for participation. For the purposes of this research, the definition proposed by Mendes is taken as the basis for analysis, which provides that

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<sup>3</sup> ‘Uploading’ as used in the research refers to the transposition of norms from one regulatory level to another. For a similar use of the term ‘uploading’ see: A. Batory, ‘Uploading as Political Strategy: the European Parliament and the Hungarian Media Law Debate’, 30(2) *East European Politics* (2014), pp. 230-245; K. Howell, ‘Uploading, Downloading and European Integration: Assessing the Europeanisation of UK Financial Services Regulation’, 6(1) *Journal of International Banking Regulation* (2004), pp. 53-68; J. Connolly, ‘Europeanization, Uploading and Downloading – The Case of Defra and Avian Influenza’, 23(1) *Public Policy and Administration* (2008), pp. 7-25.

<sup>4</sup> Livermore (2006), p. 780.

<sup>5</sup> Dorbeck-Jung (2008), p. 55.

<sup>6</sup> Möllers (2006), p. 319, p. 321.

<sup>7</sup> J. Steffek & M. Ferretti, ‘Accountability or “Good Decision”? The Competing Goals of Civil Society Participation in International Governance’, 23(1) *Global Society* (2009), pp. 37-57.

participation is to be understood as ‘procedural intervention of natural and legal persons whose substantive rights and interests are potentially affected by (...) regulatory measures, irrespective of the form in which the latter are adopted.’<sup>8</sup> In the following analysis, attention is paid to both institutionalised forms of participation, where the stakeholder forms an integral part of the institutional structure and the decision-making process, and other, less formalised forms of participation.

## 2.1 *Assessing participation in the ICH standard-setting process*

The previous chapters have shown that the ICH is to be classed as a public-private partnership, granting extensive rights and decision-making influence to industry associations. Therefore, it provides for a particularly interesting study of participatory mechanisms at the global level, as the participation of industry stakeholders in the regulatory process is an integral feature of its institutional structure. However, the participatory rights of other stakeholders still have to be examined, given that they are not inherent in the ICH institutional structure, leading to the question whether the ICH participatory mechanisms allow for a balanced input of all relevant stakeholders.

### 2.1.1 Industry participation

From its inception the ICH was constructed as a partnership between regulators and representatives of the research-based pharmaceutical industry. This partnership, and with it, the institutionalised participation of industry in the ICH standard-setting process persisted after its reform. As established in Chapter 4, both the institutional structure and decision-making process in the ICH allow for considerable participation of the pharmaceutical industry through full membership.<sup>9</sup>

Pharmaceutical industry associations are members of the ICH and are represented in the two main governing bodies, the Assembly and the Management Committee.<sup>10</sup> Moreover, they nominate experts for the Expert Working Groups,<sup>11</sup> which grants them considerable influence on the content of ICH guidelines. Although industry representatives do not have a final say in the adoption of the guidelines through the reform of the ICH decision-making process, they still contribute significantly to the scientific consensus that forms the basis of the guidelines.<sup>12</sup> Thus, the participation of the research-based industry in the process does not limit itself to an advisory role or the provision of scientific data. Industry representatives take an active part in the adoption of ICH guidelines. Although the harmonised guidelines come into being through a decision of the regulatory parties, their content is formed with significant industry input through the experts participating in the respective Expert Working Groups. Therefore, the ICH has enabled the pharmaceutical industry to directly engage with regulators in the standard-setting process, ‘influencing health care and economic decisions at the highest levels of government’.<sup>13</sup> Within the Expert Working Groups industry experts determine the scientific basis of the standards to be adopted together with experts of the regulatory authorities responsible for the marketing authorisation of medicinal products.

The establishment of the ICH as a body composed of regulators and industry is claimed to be justified through the benefits this cooperation brings for the regulators,

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<sup>8</sup> Mendes (2011b), p. 25.

<sup>9</sup> Chapter 4, Section 2.2.2, Section 3.2 and Section 4.

<sup>10</sup> Chapter 4, Section 3.2.1 and Section 3.2.2.

<sup>11</sup> Chapter 4, Section 3.2.6.

<sup>12</sup> Chapter 4, Section 4.

<sup>13</sup> Kidd (1996), p. 186.

ultimately enabling them to carry out their task not only as protectors of industrial interests, but also as guardians of public health.<sup>14</sup> Indeed, the collaboration with industry ensures that standards are set in line with the latest developments in pharmaceutical research and opens up larger resources than the public authorities could provide. This arguably enables the protection of public health through standards based on the highest expertise.

However, especially given the field in which the ICH is operational – pharmaceutical regulation, where the declared aim is a symbiosis of the protection of public health and industrial interests, which do not always overlap – the powerful representation of industrial interests in the regulatory process has attracted a lot of criticism.<sup>15</sup> This is especially precarious, given that the potentially conflicted independence is an integral feature of the ICH as a public-private partnership between regulators and the regulated industry. The role of industry stakeholders as co-regulators in the ICH should be seen in a broader context of increasing influence of the regulated industry on regulatory processes in general, where ‘commercial interests that were once regarded to be, at best, ‘troublesome’ in character, have been recast as ‘stakeholder’ (...).<sup>16</sup> Where the role of private industry actors has been redefined from being subject to regulation towards becoming active participants in the regulatory process, potential conflicts of interests are an integral feature of these new organisational forms of governance. This will be subject to further discussion in the section devoted to the independence of expertise.<sup>17</sup>

This is not to suggest that industry involvement is per se undesirable or that concerns of public health are always opposing industrial interest. Arguably, no pharmaceutical producer aims at marketing harmful products. Moreover, for the experts involved in the ICH process, their scientific reputation is at stake as well.<sup>18</sup> However, opening up public processes to participation of commercial interest requires mechanisms ensuring the transparency of these processes, which will be subject to discussion later in this chapter.<sup>19</sup> At the same time they demand a counter-balancing of industry representation through participation of the non-commercial interest representatives that the regulation seeks to protect.<sup>20</sup>

### 2.1.2 Participation of other stakeholders

While the highly institutionalised industry participation in the ICH has been assessed, the following evaluation will look beyond the industry participation to analyse whether other stakeholders also have access to the ICH decision-making process. This is particularly relevant as through ‘balancing of the interests affected by decision-making’,<sup>21</sup> participation

<sup>14</sup> Spina (2011), p. 264; A. Berman, ‘Informal International Lawmaking in Medical Products Regulation’, in A. Berman, S. Duquet, J. Pauwelyn, R. Wessel & J. Wouters (Eds.), *Informal International Lawmaking: Case Studies* (The Hague: Torkel Opsahl Academic Publishers, 2012c), pp. 353-393, p. 357.

<sup>15</sup> One of the most persistent critics of the ICH is John Abraham: Abraham & Reed (2001), pp. 113-128; Abraham (2002), pp. 1498-1502; J. Abraham & T. Reed, ‘Progress, Innovation and Regulatory Science in Drug Development: The Politics of International Standard-Setting’, 32(3) *Social Studies of Science* (2002), pp. 337-369.

<sup>16</sup> M. van Asselt, M. Everson & E. Vos, ‘The European Union Put to the Test: The Quest for Politics’, in M. van Asselt, M. Everson & E. Vos (Eds.), *Trade, Health and the Environment – The European Union Put to the Test* (Oxon/New York: Routledge/Earthscan, 2014), pp. 9-21, p. 12.

<sup>17</sup> Section 3.

<sup>18</sup> Berman (2011a), p. 55.

<sup>19</sup> Section 4.

<sup>20</sup> Scott (2010), p. 116; Möllers (2005a), p. 385; Pereira (2010), p. 569.

<sup>21</sup> Mendes (2014), p. 379.

facilitates the safeguarding of all interests protected by risk regulation policies. This is all the more important given that in its mandate the ICH acknowledges that the standards it sets aim to protect public health. Where, as argued before, the setting of regulatory standards is not only a technical/scientific but also a political exercise,<sup>22</sup> balanced stakeholder participation is needed to facilitate democratic decision-making. In order to counteract the risk of capture, an equal representation of interests in the decision-making is required.<sup>23</sup> Thus, the incorporation of diverse views in the regulation mechanisms through a system of stakeholder participation is essential to legitimate risk regulation, especially in the case of pharmaceuticals.

It should be clarified that addressing questions of stakeholder participation on the global level is subject to the presumption that direct and individual participation of citizens in global standard-setting bodies is unlikely to occur, due to a lack of capacity in terms of expertise, finance and organisational capacity.<sup>24</sup> Thus participation will take place in an imperfect form through civil society organisations such as non-governmental organizations (NGOs) and collective bodies.<sup>25</sup> Even for organised civil society, it is argued that due to financial constraints participation in global decision-making is more difficult, and that they are in a comparative disadvantage due to industrial interest representation.<sup>26</sup> In the context of pharmaceutical standards, concerned NGOs like doctors or healthcare professional associations as well as patient or consumer groups can be identified as relevant stakeholders. It needs to be acknowledged, however, that the democratic legitimisation effect of NGO participation is mitigated by the fact that participation on the global level is often only available to groups which have a specific interest and are highly organised, which means that they do not necessarily represent the interest of the general public.<sup>27</sup>

The participation of organised civil society in global standard-setting processes, like the ICH guideline-setting procedure, can take the form of either the institutionalised participation in the process itself, the form of membership or to a lesser extent through obtaining observer status, or a more externalised influence through providing comments in a public consultation procedure.

With regard to institutionalised participation mechanisms, the granting of ICH membership to NGOs would certainly be the prime mechanism to ensure participation of private, non-commercial stakeholders. However, contrary to the extensive rights granted to the industry associations in the ICH, no civil society or professionals representation group has membership status. The ICH Articles of Association limit the possibility of obtaining membership to industry and regulatory bodies.<sup>28</sup> The only institutionalised form of participation left for stakeholders other than industry associations is, therefore, observership.

In the interviews conducted for this research, the officials of the European Commission indicated that in the reform process, providing observer status to interested stakeholder organisations was considered.<sup>29</sup> And indeed, as a result of the reform process,

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<sup>22</sup> Everson & Vos (2009), p. 8.

<sup>23</sup> Ponce Solé (2011a), pp. 155-173.

<sup>24</sup> See also: Devaux (2013), p. 855; Steffek & Ferretti (2009), p. 42.

<sup>25</sup> Mendes (2011a), p. 119.

<sup>26</sup> Mendes (2011a), p. 124; Herwig (2011), p. 187.

<sup>27</sup> Mayntz (2010), p. 10; Möllers (2006), p. 321.

<sup>28</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Arts. 11 and 12.

<sup>29</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

the ICH Articles of Association now include the possibility for '(i)nternational organisations with an interest in pharmaceuticals' to obtain observer status, subject to the decision of the Assembly which acts upon recommendation of the Management Committee.<sup>30</sup> As such, observer status is inferior to full membership, as it does not provide for voting rights. It limits the participation in Expert Working Groups to occasions where the Assembly invites the observer, upon recommendation of the Management Committee, to provide experts to a specific group.<sup>31</sup> Still, obtaining observer status would allow stakeholders to closely follow the harmonisation measures proposed throughout the decision-making process, and to provide comments directly during the meetings, enabling them to actually monitor how their comments are dealt with.

At the time of writing observer status has been granted to four organisations that do not represent regulatory authorities or industry associations: the Council for International Organizations of Medical Sciences (CIOMS), the European Directorate for the Quality of Medicines & Health Care (EDQM), the International Pharmaceutical Excipient Council (IPEC), and the United States Pharmacopeia (USP).<sup>32</sup> The CIOMS is an NGO established jointly by the WHO and UNESCO representing the biomedical scientific community,<sup>33</sup> while the other organisations are engaged in the drafting of pharmacopoeias which are reference works for drug specifications (EDQM, USP)<sup>34</sup> or, in the case of the IPEC, represent producers, distributors and users of pharmaceutical excipients, thus also companies engaged in the production of pharmaceuticals in the broader sense.<sup>35</sup> Hence, only the CIOMS is representing healthcare professionals. However, other healthcare professionals as well as patients or consumers still lack representation as observers in the ICH.

As well as full observer status, it could also be conceivable that stakeholders could attend specific meetings under the status of ad-hoc observers, which was created through the adoption of the ICH Articles of Association in 2015. Ad-hoc Observer status, however, depends upon invitation through the Assembly or Management Committee.<sup>36</sup> Any natural or legal person can become an Ad-hoc Observer, however, they have to be prepared to cover their own meeting expenses<sup>37</sup> and need to be invited for each specific meeting.<sup>38</sup> This

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<sup>30</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17(1)(d) jo. 17(2).

<sup>31</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 17.

<sup>32</sup> <http://www.ich.org/about/membership.html>, last accessed: 3 April 2017.

<sup>33</sup> [www.cioms.ch](http://www.cioms.ch), last accessed: 3 April 2017.

<sup>34</sup> [www.edqm.eu](http://www.edqm.eu), last accessed: 3 April 2017; [www.usp.org](http://www.usp.org), last accessed: 3 April 2017.

<sup>35</sup> [www.ipec.org](http://www.ipec.org), last access: 3 April 2017.

<sup>36</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, Art. 18.

<sup>37</sup> However, in exceptional cases it is possible for the Assembly and Management Committee to provide some funding for the participation of ad-hoc observers. ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 14.

provision, so far, has not been used for civil society or professional association stakeholders.<sup>39</sup>

Accordingly, through the ICH reform process, institutionalised participation has been opened up for non-industry stakeholders. However, if the commitment to balanced participation is taken seriously, health interests groups should be able to obtain full membership rights, thereby making the institutional structure of the ICH truly representative of its dual mandate: the protection of public health and industry interests. Since granting the observer status does not provide them with a right to vote, this can only counterbalance the industries' membership rights to a certain extent. Finally, it should also be mentioned that the representation of public health interests in the ICH procedure is secured indirectly through the regulatory authorities and their dual mandate to promote public health, while also paying due attention to industrial interests.

While some claim that the apparent exclusion of other societal interests in pharmaceutical regulation is steered by the pharmaceutical industry,<sup>40</sup> the budgetary constraints that public interest advocacy groups possibly also face has an impact on their inability to establish themselves as a major global political force like the industry successfully did.<sup>41</sup> In this context, an EFPIA official pointed out that if there would be an institutionalised role of civil society organisations, the question would be whether they would have the financial means to participate in the process. This entails attending the bi-annual ICH week including covering the travelling costs, and whether they would even be interested in participating in all harmonisation activities sending experts to working groups.<sup>42</sup>

When considering other, less institutionalised mechanisms of stakeholder participation in the ICH standard-setting process, the primary possibility for non-commercial stakeholders in the current ICH process is the public consultation in the third step of the ICH standard-setting process.<sup>43</sup> The consultation is carried out through the regulatory authorities with ICH membership applying their public consultation mechanisms, and through the ICH website.<sup>44</sup> Being open to everyone interested, comments can be provided to the regulatory authorities of the three regions or the ICH Secretariat.<sup>45</sup>

However, the public consultation takes place only after the scientific consensus is formed and shortly before the adoption of the guideline, which is quite late in the process. It

<sup>38</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 9.

<sup>39</sup> The provision was used in 2016 to allow the participation of the Chinese Food and Drug Administration (CFDA), in the June and November 2016 Assembly, and of the Pharmaceutical Inspection Co-operation Scheme (PIC/S), during the June 2016 Assembly. See: ICH, Meeting Minutes ICH Assembly November 9-10 2016, Osaka, Japan, 2 February 2017, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/Ass\\_MC\\_Meetings\\_Reports/Assembly\\_report\\_Osaka\\_2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/Ass_MC_Meetings_Reports/Assembly_report_Osaka_2016.pdf), last accessed: 3 April 2017; ICH, Meeting Minutes ICH Assembly June 15-16 2016, Lisbon, Portugal, 20 September 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/Ass\\_MC\\_Meetings\\_Reports/Assembly\\_report\\_Lisbon\\_2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/Ass_MC_Meetings_Reports/Assembly_report_Lisbon_2016.pdf), last accessed: 3 April 2017.

<sup>40</sup> Abraham (2002), p. 1500.

<sup>41</sup> See also: Dorbeck-Jung (2008), p. 56.

<sup>42</sup> Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>43</sup> For the ICH five-step decision-making procedure see Chapter 4, Section 4.

<sup>44</sup> Chapter 4, Section 4.

<sup>45</sup> The ICH public consultation webpage is: <http://www.ich.org/products/open-consultation.html>, last accessed: 3 April 2017.

is questionable how much effect the comments will have at this late stage of the guideline procedure and whether the parties are truly open to deviate from the position they have already negotiated. The harmonisation procedure foresees that the comments received through the public consultation are discussed in the Expert Working Group,<sup>46</sup> however, from an external perspective it cannot be tracked whether this indeed happens and to what extent. This hinders the meaningful provision of comments by stakeholders as they receive no feedback enabling them to engage in active discussions. It certainly has a demotivating effect, as the impact of the comments is not visible and unsure.<sup>47</sup> Therefore, although the public consultation procedure opens the door to participation of societal interest, the possibilities for actual influence on the procedural outcome conveyed through this are limited.

Conclusively, the participatory mechanisms in the ICH operate mainly in favour of the participation of industrial interest, whereas other stakeholders only have limited access to the standard-setting. These heavily imbalanced participation options fall short of the overall aim of pharmaceutical regulation, which consists of the protection of public health as well as the consideration of economic interests. This is unfortunate as the incorporation of all relevant interest, next to legitimacy benefits, also contributes to the factual acceptance of standards in practice. It also helps to substantially improve them, as doctors and patients in particular dispose of practical knowledge that can benefit the rule-making.<sup>48</sup> For instance, the ICH Guideline on Good Clinical Practice<sup>49</sup> that is concerned with clinical trials from a scientific but also an ethics perspective (such as through requiring the establishment of independent ethics committees), has been developed largely without the involvement of patient and consumer or professional groups, leading to criticism of this practice by the respective non-profit groups.<sup>50</sup>

It is, therefore argued by some authors that the involvement of industry without representation of other interests is highly problematic, as the efficiency of the ICH might be owed to the marginalisation of non-industrial interests.<sup>51</sup> Although in principle, cooperation with private stakeholders can certainly have a positive influence on the quality of decision-making, due to the expertise provided by private profit and nonprofit parties, it becomes an obstacle to legitimate regulation. Private interests become factually synonymous with commercial interests, and are not counterbalanced with the sufficient involvement of other interested parties.

## 2.2 *EU perspective: EMA and the principle of participation*

Having established the shortcomings in the participatory mechanisms at the ICH level, it is now time to look at participation rights and opportunities in EU pharmaceutical regulation. The guideline drafting procedure as applied by the European Medicines Agency will be looked at specifically in order to evaluate the findings with regard to the ICH from an EU perspective. Chapter 2 established that participatory openness is enshrined in the Treaties through Articles 10 and 11 of the TEU as well as Article 15 TFEU, making it a general

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<sup>46</sup> ICH, Standard Operating Procedures for the ICH Working Groups, p. 17.

<sup>47</sup> See also: Mendes (2012), p. 1013.

<sup>48</sup> Livermore (2006), p. 780.

<sup>49</sup> ICH, ICH Harmonised Tripartite Guideline – Guideline for Good Clinical Practice E6, 10 June 1996.

<sup>50</sup> WHO, 'International Harmonization of Regulatory Activities: Future Options', 14(3) *WHO Drug Information* (2000), p. 147.

<sup>51</sup> Abraham & Lewis (2000), p. 138.

European constitutional principle.<sup>52</sup> Article 11 TEU contains an obligation for open and regular dialogue and contains the duty for the Commission to hold stakeholder consultations. While this duty does not extend to agencies, Article 15 TFEU does require the openness of agency work in order to facilitate civil society participation. Together with the fact that Article 11 TEU links participation to democracy, a founding value of the EU, this means that agencies are not free to disregard the participation requirement established by the general principles of EU law.<sup>53</sup> In this regard the European Parliament's proposal for an EU administrative procedure law stresses the importance of a balanced approach to stakeholder participation, as it explicitly requires that the EU's 'administration shall guarantee a fair balance between different types of citizens' interests (business, consumer and other)'.<sup>54</sup>

Stakeholder participation is enshrined in the institutional structure of the EMA. In the EMA Management Board, two members represent patients' organisations and, additionally, the board includes one representative of a doctor's association and one representative of a veterinarian's association, which provides these representatives with considerable influence on the work of the agency.<sup>55</sup> In addition to that, patients' and consumers' organisations have representatives in several EMA Committees (the Committee for Orphan Medicinal Products (COMP), the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmacovigilance and Risk Assessment Committee (PRAC)).<sup>56</sup> Furthermore, health care professionals are represented in the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT), and the Pharmacovigilance and Risk Assessment Committee (PRAC).<sup>57</sup>

This participatory openness is also reflected in the founding regulation of the EMA, which provides that the Management Board has to 'develop appropriate contacts between the Agency and the representatives of industry, consumers and patients and the health professions',<sup>58</sup> which may take the form of 'the participation of observers in certain aspects of the Agency's work, under conditions determined beforehand by the Management Board'.<sup>59</sup> All these policies have to be developed in agreement with the Commission.<sup>60</sup> Moreover, the EMA's Scientific Committees and their working parties and advisory groups 'shall in general matters establish contacts, on an advisory basis, with parties concerned with the use of medicinal products, in particular patient organisations and health-care professionals' associations'.<sup>61</sup> Thus, in its general activities the agency is obliged to maintain

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<sup>52</sup> Chapter 2, Section 5.2.

<sup>53</sup> Chapter 2, Section 5.2.

<sup>54</sup> European Parliament, Resolution of 15 January 2013 with recommendations to the Commission on a Law of Administrative Procedure of the European Union (2012/2024(INL)), P7\_TA(2013)0004, Recommendation 3. See also: E. Vos, 'EU Agencies and Independence', in D. Ritleng (Ed.), *Independence and Legitimacy in the Institutional System of the European Union* (Oxford: Oxford University Press, 2016), pp. 206-228, p. 214f.

<sup>55</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 65.

<sup>56</sup> EMA, Revised framework for interaction between the European Medicines Agency and patients and consumers and their organisations, EMA/637573/2014, 16 October 2014, p. 3.

<sup>57</sup> EMA, Working with healthcare professionals, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Leaflet/2013/03/WC500140714.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2013/03/WC500140714.pdf), last accessed: 3 April 2017.

<sup>58</sup> Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 348, 31 December 2010, pp.1-16, Art. 78(1).

<sup>59</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 78(1).

<sup>60</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 78(1).

<sup>61</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 78(2).

contacts with its stakeholders, and has institutionalised the participation of stakeholders in several ways.

The Management Board adopted a 'Revised framework for interaction between the European Medicines Agency and healthcare professionals'<sup>62</sup> as well as a 'Revised framework for interaction between the European Medicines Agency and patients and consumers and their organisations'.<sup>63</sup> Nowadays the EMA has established a network of healthcare professionals associations as well as the so-called Healthcare Professionals Working Party (HCPWP).<sup>64</sup> This working party provides a forum for the dialogue between the professionals' associations and the agency including its Committees, also providing feedback on various aspects of the agencies' work.<sup>65</sup> The Patients' and Consumers' Working Party (PWCP), which has been operational since 2006, is contributing to the work of the agency and its Committees through recommendations, together with a network of patients' and consumers' organisations.<sup>66</sup> Thus, the agency has made significant efforts to provide participation opportunities for civil society actors. In contrast to the ICH, here the participation of non-industry interests is institutionally strengthened, whereas the industry involvement is less formalised.<sup>67</sup> Therefore, whereas mechanisms for stakeholder involvement often run the risk of favouring those with high expert capacity and financial resources such as the regulated industry,<sup>68</sup> the EMA has set up a framework to actively support less powerful civil society actors in their participation efforts.

Of high importance for this research is the role of stakeholders in the drafting of guidelines. As the ICH guidelines become EMA guidelines after implementation, it is relevant to examine how EMA guidelines are adopted when they do not originate in the ICH process but solely in the EMA itself, and which role stakeholders play in the adoption of these EMA originating guidelines.

As far as the Commission is concerned, Art. 31(4) of Regulation 726/2004 provides that when drafting guidelines establishing the form of marketing authorisation applications, the Commission should work together with the agency, Member States and interested stakeholders. Regulation 726/2004 does not contain a similar provision for the adoption of EMA guidelines; however, the EMA has adopted an elaborate guideline adoption procedure.<sup>69</sup> In the 10-step guideline drafting process by the EMA, stakeholder participation is mainly facilitated through public consultation.<sup>70</sup> In step 4, a concept paper, which contains the matters that have to be addressed and the expected impact of the guideline on regulators,

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<sup>62</sup> EMA, Framework for interaction between the European Medicines Agency and health care professionals, EMA/688885/2010, 15 December 2011.

<sup>63</sup> EMA, Revised framework for interaction between the European Medicines Agency and patients and consumers and their organisations, EMA/637573/2014, 16 October 2014.

<sup>64</sup> EMA, Framework for interaction between the European Medicines Agency and health care professionals, EMA/688885/2010, 15 December 2011, p. 7.

<sup>65</sup> EMA, Framework for interaction between the European Medicines Agency and health care professionals, EMA/688885/2010, 15 December 2011, p. 8.

<sup>66</sup> EMA, Revised framework for interaction between the European Medicines Agency and patients and consumers and their organisations, EMA/637573/2014, 16 October 2014, p. 6ff.

<sup>67</sup> EMA, Framework for interaction between the European Medicines Agency and industry stakeholders, EMA/591272/2014, 2 October 2015.

<sup>68</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 47.

<sup>69</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 9f.

<sup>70</sup> For a full description see Chapter 5, Section 2.

regulatees and interested parties, is released for a two to three month public consultation.<sup>71</sup> The Patients' and Consumers' Working Party will help develop the proactive consultation with patient's and consumer's associations.<sup>72</sup> The comments received will be taken into account in the guideline drafting process in step 5.<sup>73</sup> Then, once the draft guideline has been developed by the working party and is adopted by the responsible committee or other EMA organ, it is released for public consultation again for a period of three to six months.<sup>74</sup> The comments are subsequently discussed in a drafting group and will be published on the consultation website (unless issues of commercial confidentiality arise or the authors object to the publication).<sup>75</sup> Furthermore, the rapporteur prepares an overview of comments received and includes notes on whether the comments have been taken into account or not, which will also be published and remain accessible through the archive of the EMA website.<sup>76</sup> Moreover, throughout the process, meetings might be organised with stakeholders for further discussions.<sup>77</sup> Additionally, in the 'Road map to 2015' it was emphasised that in the guideline drafting process stakeholder participation should also be enhanced, for instance through organising workshops at the beginning of the guideline drafting procedure.<sup>78</sup>

The main difference of the EMA procedure when compared to the ICH procedure is the two-stage public consultation procedure in the process. As the EMA, after incorporating the comments received in the first consultation round, opens up the document for public consultation again, stakeholders can give feedback on the implementation of their comments. This encourages a dialogue between the regulator and the private interest stakeholders. Moreover, the practice of the European Medicines Agency to publish a summary overview of the comments received including short responses to them, shows that the comments have indeed been considered, and also provides a short explanation for why they have been incorporated or not. Moreover, this makes the public consultation more transparent, as it becomes visible who has provided which comments. This stands in sharp contrast to the ICH guideline adoption procedure where once the comments are submitted to the ICH, they leave no trace that could be followed by external stakeholders. The EMA

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<sup>71</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 11.

<sup>72</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 11.

<sup>73</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 11.

<sup>74</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 12.

<sup>75</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 13.

<sup>76</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 13.

<sup>77</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 9f.

<sup>78</sup> EMA, Road map to 2015 – The European Medicines Agency's contribution to science, medicines and health, Adopted by the Agency's Management Board on 16 December 2010, p. 18.

consultation procedure is by far more transparent.<sup>79</sup> The EMA facilitates the involvement of patients, consumers and healthcare professionals, mainly through their respective organisations, both in its institutional structure and the specific guideline drafting procedure, while the ICH only provides very limited participation mechanisms. The Commission has pointed out that the ICH process is already very cumbersome through the consensus requirement and that additional steps, like publishing a summary with responses to comments – which again would have to be agreed upon by consensus – would be counterproductive.<sup>80</sup>

When the EMA implements the ICH guidelines all these procedural efforts to facilitate stakeholder involvement are not made. The public consultation procedure is carried out by the EMA, although it does not follow all the steps of its own guideline adoption procedure. While the EMA publishes summaries of the comments of its public consultations, it does not do so systematically with regard to the public consultations of draft ICH guidelines.<sup>81</sup> Also the ICH itself neither provides access to the comments received by its regulator members and submitted directly to the ICH, nor does it provide reasons for either taking into account or disregarding comments.

Overall, significant differences between the participatory openness for stakeholders can be identified between the drafting of ICH guidelines and the drafting of analogous guidelines adopted by the EMA in the purely EU-based procedure, both with regard to institutionalised forms of stakeholder participation and in the public consultation procedures. The response to comments the EMA received in the process of adopting its own guideline procedure is very remarkable. Confronted with the suggestion that more industry involvement should be facilitated, similar to the ICH mode of decision-making, the

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<sup>79</sup> See also: Mendes (2012), p. 1013.

<sup>80</sup> Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015.

<sup>81</sup> Recently, in February 2017, the EMA published the comments it received in the public consultation procedure for the ICH E17 guideline. (See: EMA, Overview of comments received by EMA on 'ICH guideline E17 on general principles for planning and design of multi-regional clinical trials – Step 2b', EMA/CHMP/ICH/453276/2016, 10 February 2017, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Overview\\_of\\_comments/2017/02/WC500221551.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2017/02/WC500221551.pdf), last accessed: 3 April 2017.) It also published comments received in the consultation procedures for two ICH Q&A documents. (See: EMA, Overview of comments received by EMA on 'ICH guideline Q11 on development and manufacture of drug substances (chemical entities and biotechnological/biological entities) – questions and answers, EMA/CHMP/809509/2016, 21 March 2017, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Overview\\_of\\_comments/2017/03/WC500224269.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2017/03/WC500224269.pdf), last accessed: 3 April 2017; EMA, Overview of comments received by EMA on 'Questions and answers – ICH S9 guidelines on nonclinical evaluation for anticancer pharmaceuticals – Step 2b', EMA/CHMP/ICH/454684/2016, 10 February 2017, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Overview\\_of\\_comments/2017/02/WC500221552.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2017/02/WC500221552.pdf), last accessed: 3 April 2017.) However, these are very recent developments and it is unclear whether this indicates the introduction of a general policy of the EMA, to publish comments it receives in public consultations carried out for ICH guidelines and other documents. Should this be the case, such a development should be welcomed in the context of increasing participatory openness and transparency. However, it should also be noted that the publication only concerns comments received by the EMA and not the comments received by other ICH members or the ICH centrally. Furthermore, in contrast to the overview of comments published for non-ICH EMA guidelines, the document does not contain responses of the Agency, addressing the comments received.

EMA stressed the need to consider all relevant stakeholders and not just industry interests, in stating:

‘The procedure takes over many aspects of the ICH/VICH model. However it does not propose to systematically involve industry in all steps of the process, nor does it propose that industry would draft guidelines. In view of the need to have a harmonised position among all 25-member states, systematic early involvement of industry would not be appropriate. (...) Overall there are plenty of opportunities for industry to comment. Drafting suggestions from industry are always welcomed but careful consideration has also to be given to equal treatment of all relevant interested parties during the procedure.’<sup>82</sup>

It is remarkable that early industry involvement without balancing it with the participation of other interest representatives according to the EMA is not acceptable in the procedure harmonising the standards on the EU level. At the same time it is established practice in the harmonisation of standards on the global level, which once they are implemented have the same status as other EMA guidelines in the Member States. Whereas implemented ICH guidelines and guidelines originating in the agency itself are not distinguished in the pharmaceutical regulatory framework, their drafting process varies considerably from a participatory perspective.

### 2.3 *Uploading EU administrative law: Participation*

The previous analysis has shown that the institutional and procedural differences between the ICH and the EU standard-setting work to the detriment of civil society and public health interests on the global level. On the ICH level, non-commercial stakeholders in contrast to industry associations are excluded from membership. They are limited to observer status. Moreover, the ICH public consultation procedure shows several disadvantages for stakeholder participation when compared to the EU procedure.

Lessons can be learned from the EMA guideline adoption procedure that could lead to more balanced stakeholder participation in the ICH. First of all, the EMA has institutionalised the participation of the often less powerful non-commercial stakeholders in its internal bodies and in the guideline adoption procedure. Opening up the observer status to potential access by NGOs was a first step into this direction. However, overall, the participation of stakeholders could be promoted through establishing a specialised body within the ICH – comparable to the EMA Patients’ and Consumers’ Working Party or the Healthcare Professionals’ Working Party – actively engaging and liaising with healthcare professionals and consumer organisations.

Effective stakeholder participation might then also require the provision of funding possibilities for NGO members to counterbalance the financial disadvantage they have as opposed to the industry. The process of setting ‘European standards’ by private bodies, mentioned in Chapter 1, could provide an example.<sup>83</sup> Concerns of lacking stakeholder participation in the creation of European standards by private standard-setters were addressed by funding stakeholder organisations through the EU budget.<sup>84</sup> These stakeholder

<sup>82</sup> EMA, Overview of comments received on draft guideline procedure for EU guidelines and related documents within the pharmaceutical legislative framework, EMEA/125817/2004.

<sup>83</sup> Chapter 1, Section 2.2.

<sup>84</sup> Currently the EU financially supports three organizations in the context of European standardization: The European consumer voice in standardization (ANEC), European Trade Union Confederation (ETUC), and European Environmental Citizens’ Organisation for

organisations subsequently participate in the development of European standards.<sup>85</sup> Thus, it might be conceivable that with its membership financed budget the ICH could set aside resources to fund stakeholder organisations representing private interests like professionals, patients or civil society organisations. However, this would also make these stakeholders dependent on the partially industry-financed ICH budget, which might compromise their independence.

When it comes to more procedural aspects, what certainly can be improved on the basis of the EMA guideline adoption procedure is the public consultation process the ICH carries out. The fact that draft guidelines are opened for consultation at two different steps in the EMA procedure, whereas the first round of consultation is carried out early in the adoption process, facilitates more meaningful interaction with interested stakeholders. This could be carried out in the ICH standard-setting procedure by already submitting the concept paper that is adopted at the start of a harmonisation activity to an additional public consultation procedure. Moreover, the ICH should centrally publish a summary of all comments received in the public consultation, including the ones it received directly as well as the ones received by the regulatory members. Such a summary would then benefit from short responses as to the position of the ICH towards the comments received, as this would assure stakeholders that their comments are taken into account and also enable a dialogue between the ICH and the stakeholders, ultimately facilitating a learning process on both sides.

It was pointed out that the fact that the ICH is established as a regulator-industry partnership means that naturally the context in which participation is discussed is fundamentally different from the EU context, where the EMA is discussing the guidelines as a public body. What, however, can be deduced from EU administrative law is that participation should be open to all interested stakeholders. Against this background, truly balanced participatory openness would require that membership of the ICH should be opened up to other stakeholders than industry.

### 3. INDEPENDENT EXPERTISE

In Chapter 1 it was established that expertise and resources offered by the industry often constitute the trigger for regulating in the form of a public-private partnership in order to address the complex risks faced by society today.<sup>86</sup> It is presumed that integrating the technical and scientific knowledge of experts into regulatory processes is necessary for efficient regulation. These experts are supposed to contribute their knowledge in a manner that is ‘objective, neutral and independent’.<sup>87</sup>

In a scientific and technical area such as that of pharmaceuticals, the industry attracts highly skilled experts and, through conducting the research necessary for drug development, these industry experts have the finger on the pulse of time when it comes to innovation.<sup>88</sup> Through including the pharmaceutical industry in a harmonisation process the regulators get

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Standardization (ECOS). This financial support is based on Regulation (EU) No 1025/2012 of the European Parliament and of the Council of 25 October 2012 on European standardisation, OJ L 316, 14 November 2012, pp. 12-33.

<sup>85</sup> Regulation (EU) No 1025/2012 of the European Parliament and of the Council of 25 October 2012 on European standardisation, OJ L 316, 14 November 2012, pp. 12-33, Art. 5.

<sup>86</sup> Chapter 1, Section 4.1.2.

<sup>87</sup> Devaux (2013), p. 848.

<sup>88</sup> See also: Berman (2011a) p. 22ff.

access to data, which they otherwise would not be aware of.<sup>89</sup> The reliance on industry expertise, however, becomes problematic where ‘the borderlines between the pursuit of commercial self-interest and the provision of expertise are often blurred’.<sup>90</sup> This is especially critical since it is widely acknowledged that risk regulation, although presented as based on the rock of ‘science’, is highly porous for various other influences.<sup>91</sup> Thus, although the epistemic legitimacy of global standard-setting bodies is often a reason for their establishment being a success,<sup>92</sup> their expertise should not be contemplated as detached from the potential influences that these bodies might be subject to.

In terms of good governance values and legitimate standard-setting, participants in the decision-making process should be prevented from benefitting from steering the regulation into a certain direction.<sup>93</sup> Therefore, the independence requirement is closely related to the participation of stakeholders, and specifically of industry representatives, as discussed in the previous section. It also extends to the regulatory participants in the standard-setting process, and whether they are independent or have personal interests in the pharmaceutical industry.

### 3.1 *Assessing expertise in the ICH in terms of independence*

The independence of expertise within the ICH, as it is organised as a partnership between the regulators and the pharmaceutical industry, leads to challenges per se in terms of independence, as the standard-setting process heavily relies on the input of the regulated industry. Prohibiting industry experts from taking part in the standard-setting process within the ICH system, in order to ensure the scientific objectivity of the standards, would of course go against the entire logic of this public-private partnership. In this regard, where public-private partnerships allow for co-regulation by the regulated industry, there is an inherent risk that the rules agreed upon might be intentionally debilitated by those who would have to comply with them in the first place.<sup>94</sup>

However, whereas the integration of industry expertise in the ICH process is inherent in its organisational structure and decision-making process, it is noticeable that in the ICH no effort is undertaken to address potential conflicts of interest through other means than a full prohibition of industry participation in the ICH process. In his speech during the first International Conference on Technical Harmonisation, Commissioner Bangemann presented the ICH as a forum where ‘real experts can express the true scientific needs and the regulators can benefit from the clear unbiased view of these international experts’.<sup>95</sup> Given the role of the industry as an important partner in the ICH decision-making process, with no restrictions with regard to experts which might have commercial interests in the harmonisation topic at stake, this statement is a rather naïve perspective on expertise.

Since the ICH reform, industry representatives are prohibited from voting on the adoption of a new topic in the Assembly and are also excluded from the final decision-

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<sup>89</sup> Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>90</sup> Quack (2010), p. 10.

<sup>91</sup> Jasanoff (2013), p. 133.

<sup>92</sup> As Berman points out, the ICH is viewed as having broad ‘epistemic legitimacy’ in the sense that the standards are scientifically up to speed, which explains their global influence. Berman (2011a), p. 55.

<sup>93</sup> Esty (2005-2006), p. 1524ff.

<sup>94</sup> Börzel & Risse (2007), p. 210.

<sup>95</sup> Bangemann (1992), p. 5.

making when the guidelines are adopted.<sup>96</sup> However, in the Expert Working Groups, which establish the content of the guidelines, there is no conflict of interest policy which would require experts to declare their interests and attach consequences to existing conflicts. Realising that in the public-private standard-setting bodies the parameter should not be whether there are conflicts of interest, but rather how they are dealt with, the following questions arise: are the affiliations and interests of the experts involved communicated within the body? Are they communicated to the outside world? Is any consequence attached to conflicts of interest of individual experts participating in the forming of scientific consensus?

Admittedly, dealing with conflicts of interest in public-private settings is challenging. However, a transparent handling of existing interests at least is a prerequisite for legitimate standard-setting. The representatives participating in the Assembly and the Management Committee are listed on the ICH website, including their affiliation.<sup>97</sup> This is important, given that some members representing industry associations are directly employed by pharmaceutical companies.<sup>98</sup> However, the membership of the working groups is not made public and the Standard Operating Procedures for the ICH Working Groups document does not reveal any criteria for the choice of experts for the working groups.<sup>99</sup> It therefore remains impossible to comprehend who has been involved in the drafting of the guidelines and in what way the expert might have had an interest in interfering with the harmonisation outcome.

Leaving aside the communication of possible conflicts to the outside world, from the information publicly available there also seems to be no internal policy on conflicts of interest. One could for example think about whether the affiliation of individual experts in the working groups is communicated to the other members, so that everyone in the discussion is aware that opinions might have to be evaluated in the light of the person's interests. Whether the experts with industry interest have indeed been successful in influencing ICH standards in a direction they desired is difficult to establish without scientific expertise. However, Abraham claims several instances where the ICH has opted for the less strict standard within the regulatory options available.<sup>100</sup>

### 3.2 *EU perspective: EMA and the principle of independent expertise*

The independence of expertise is an important value in the EU administrative law governing risk regulation.<sup>101</sup> Article 298 TFEU provides for an 'open, efficient and independent European administration'. Also in the *Pfizer* case, which was very influential on the EU's risk

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<sup>96</sup> Chapter 4, Section 4.1.

<sup>97</sup> For the list of members of the ICH Assembly see: <http://www.ich.org/about/organisation-of-ich/coopgroup.html>, last accessed: 3 April 2017; for the list of members of the Management Committee see: <http://www.ich.org/about/organisation-of-ich/steering.html>, last accessed: 3 April 2017.

<sup>98</sup> For example, the EFPIA Representative in the Management Committee, Dr. Sabine Luik, is employed at Boehringer Ingelheim Pharmaceuticals. See: <http://www.ich.org/about/organisation-of-ich/steering.html>, last accessed: 3 April 2017.

<sup>99</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016.

<sup>100</sup> Abraham (2002), p. 1500.

<sup>101</sup> For a detailed analysis of Independence with regard to EU Agencies see: Vos (2016), pp. 206-228.

regulation, the Court required that risks must be assessed by experts based on the ‘principles of excellence, independence and transparency’.<sup>102</sup>

The Code of Good Administrative Behaviour, as developed by the Ombudsman and endorsed by the Parliament, requires officials to ‘be impartial and independent’<sup>103</sup> and to ‘abstain from (...) any preferential treatment on any grounds whatsoever’.<sup>104</sup> A similar provision is also included in the European Parliament’s proposed EU administrative procedure law.<sup>105</sup> The European Medicines Agency, with a reference to the Code of Good Administrative Behavior of the Ombudsman, has adopted its own Code of Good Administrative Behavior,<sup>106</sup> which states that:

‘The staff of the Agency shall be impartial and independent, and respect principles of scientific integrity. They shall abstain from any arbitrary action adversely affecting members of the public or the Agency’s stakeholders, as well as from any preferential treatment on any grounds whatsoever.

The staff of the Agency shall not be guided by any outside influences of whatever kind, including political or national influences, or by personal interests. They shall abstain from being involved in the taking of a decision on a matter concerning their own interests, or those of their family, relatives, and/or friends. In performing their role within the context of the Agency’s work scientific independence shall be ensured.’<sup>107</sup>

Independence of expertise is a prerequisite for creating legitimate standards, this especially so in an area where public health and industrial interests both deserve protection. European agencies should encompass both the independence from political influence through other EU institutions as well as from Member States, but also from players in the respective regulated field.<sup>108</sup>

As a core principle in risk regulation, independence from the regulated industry has been enshrined in European pharmaceutical legislation too. Article 62(3) of Regulation 726/2004 prohibits members of the EMA’s Management Board, committee members, and external experts consulted by the agency from having any financial or other interest in the pharmaceutical industry. Indirect interests have to be declared and published in a register. Direct interests are defined by the agency as employment with, consultancy to, or an

<sup>102</sup> Case T-13/99 *Pfizer Animal Health v. Council*, ECLI:EU:T:2002:209, para. 159.

<sup>103</sup> European Ombudsman, Code of Good Administrative Behaviour, 2015 (updated edition), Art. 8, available via: <http://www.ombudsman.europa.eu/en/resources/code.faces#/page/1>, last accessed: 3 April 2017; European Parliament, Resolution A5-0245/2001 on the European Ombudsman’s Special Report to the European Parliament following the own-initiative inquiry into the existence and the public accessibility, in the different Community institutions and bodies, of a Code of Good Administrative Behaviour (C5-0438/2000 – 2000/2212 (COS)), 6 September 2001.

<sup>104</sup> European Ombudsman, Code of Good Administrative Behaviour, 2015 (updated edition), Art. 8.

<sup>105</sup> European Parliament, Resolution of 15 January 2013 with recommendations to the Commission on a Law of Administrative Procedure of the European Union (2012/2024(INI)), P7\_TA(2013)0004, Recommendation 3.

<sup>106</sup> EMA, The European Medicines Agency Code of Good Administrative Behaviour, EMA/264257/2013, 1 September 2013.

<sup>107</sup> EMA, The European Medicines Agency Code of Good Administrative Behaviour, EMA/264257/2013, 1 September 2013, p. 4.

<sup>108</sup> Vos (2014), p. 37. For the EMA experts this is enshrined in Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 61(6) jo Art. 63.

advisory role for a pharmaceutical company, as well as financial interests or intellectual property rights.<sup>109</sup> Indirect interests are defined as the principal investigator, or clinical trial investigator, working for an institution or organisation sponsored by the industry.<sup>110</sup> This also covers the three years preceding the time of taking up the activity at the EMA.<sup>111</sup> Where the respective person either has or had an executive role in a pharmaceutical company or a leading role in the development of a medicinal product, these will have to be declared indefinitely.<sup>112</sup> These declarations of interest are updated at least annually or whenever the interests change.<sup>113</sup> According to a standard operating procedure for scientific meetings, these declarations are assessed before every meeting in order to assign the necessary restrictions and to inform all meeting participants about the conflict of interest status of the participants.<sup>114</sup> The conflict of interest rules apply to all members of the scientific committees including the alternates, and to experts, explicitly regarding all activities of the agencies, including the drafting of guidelines.<sup>115</sup> Additionally, similar rules have applied to all staff members of the agency since 2012, committing them to fill out their declarations of interest.<sup>116</sup>

Especially interesting for the discussion in relation to the ICH is how the EMA deals with experts, committee members or staff members that have declared conflicts of interest. Here, an EMA policy has been put into place, which essentially consists of assigning a risk level to respective person. According to that the activities of the person in the EMA work are restricted, also taking into account the specific task in the agencies work in question.<sup>117</sup> Current employment or financial interest within the pharmaceutical industry will exclude the person from participating in the work of the agency.<sup>118</sup> For all other declared conflicts of interest, the respective person might be excluded from procedures regarding a specific product, or might be allowed to take part in the discussion but not the final deliberation. This will depend on the declared interest in question and the role of the person concerned in

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<sup>109</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 3f.

<sup>110</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 4f.

<sup>111</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 8.

<sup>112</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 7.

<sup>113</sup> EMA, The European Medicines Agency Code of Conduct, EMA/385894/2012 rev.1, 16 June 2016, p. 7.

<sup>114</sup> EMA, Standard operating procedure: Arrangements for handling of conflicts of interest for EMA scientific meetings, SOP/EMA/0126, 8 October 2012.

<sup>115</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 2.

<sup>116</sup> EMA, Decision on rules relating to Articles 11a and 13 of the Staff Regulations concerning the handling of declared interests of employees of the European Medicines Agency, 1 February 2012, EMA/MB/500408/2011. Now replaced by: EMA, Decision on rules relating to Articles 11, 11a and 13 of the Staff Regulations concerning the handling of declared interests of staff members of the European Medicines Agency and candidates before recruitment, EMA/259494/2016, 6 October 2016.

<sup>117</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016.

<sup>118</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 8.

the process.<sup>119</sup> The policy even takes into account whether close family members are working in the pharmaceutical industry and imposes restrictions on persons where this is the case.<sup>120</sup> Where a committee member or expert with restrictions has taken part in a meeting this will be recorded in the minutes of the meeting which are published on the website, which increases the transparency of conflicts.<sup>121</sup>

One should, however, also mention that in the past the European Medicines Agency has been criticised for conflicts of interest, especially from the European Parliament.<sup>122</sup> It has since then updated its conflict of interest policy extensively, as the previous analysis has reflected on. Nonetheless, ensuring independence, especially from commercial interests, is very much a work in progress for the EMA. The agency has resorted to publishing an annual review of its policy on independence, which also contains recommendations for improvement and indicates further initiatives the Agency will undertake.<sup>123</sup> Thus, also in the EMA, the handling of conflicts of interest still leaves room for improvement. The agency has also acknowledged its difficulty in balancing a strict conflict of interest policy with finding the much-needed expertise.<sup>124</sup>

### 3.3 *Uploading EU administrative law: Independent expertise*

First of all, it is important to again underline the core value of the principle of independent expertise, especially for pharmaceutical regulation, which is inherently aimed at protecting public health as a common good. Nonetheless it also needs to be acknowledged that the expertise required for carrying out these regulatory tasks often requires relying on experts who are either current or former employees of the pharmaceutical industry. Therefore, a system of identifying and addressing these conflicts is important, especially in this regulatory area.

Applying the EMA conflict of interest system to the ICH would mean that the standard-setting based on consensus in partnership with industry would be prevented by the conflicted interest of the industry representatives involved. Thus with the form of the public-private partnership, the arising of conflicts of interest with regard to the participants from the industry associations is inherent. A solution would require excluding the industry associations from membership. This would therefore fundamentally restructure the ICH's public-private character. Although this would be essential from the perspective of the core principle of independence, in practice this does not seem likely to occur in the near future, given the legacy of the ICH.

Still, lessons should be learned from the EMA's conflict of interest policy where the aim would be to maintain the public-private partnership. Publicly accessible conflict of interest declarations would make conflicts visible to the other ICH members as well as

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<sup>119</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 7f.

<sup>120</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 12.

<sup>121</sup> EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee's members and experts, EMA/626261/2014 Rev.1, 6 October 2016, p. 9.

<sup>122</sup> European Parliament, Decision of 10 May 2012 in Discharge in Respect of the Implementation of the Budget of the European Medicines Agency for the Financial Year 2010, (C7-0281/2011 – 2011/2220 [DEC]).

<sup>123</sup> See: EMA, 2015 Annual report on independence, EMA/175527/2016, 16 September 2016.

<sup>124</sup> EMA, Best expertise vs conflict of interests: Striking the right balance, Report from the public workshop hosted by the European Medicines Agency in London on 6 September 2013, EMA/548247/2013, p. 2.

external stakeholders. This would at least make the industrial interests in the development of a specific guideline more transparent. Thus, a first step to enhance the ICH's approach to conflicts of interest would be to make them visible, internally and externally, with declarations of interest of everyone taking part in the ICH activities publicly available on the website. Moreover, it is also necessary to make visible in which meetings certain persons with conflicted interests have participated. Nonetheless, it has to be concluded that the core nature of the ICH as a hybrid body stands in irreconcilable contrast to the conflict of interest policies as applied to guidelines developed by the EMA itself. This could be mitigated through a more transparent conflict of interest policy, but the fundamental problem remains. This leads to serious concerns with regard to the legitimacy of the ICH standards and also undermines the rules applicable within the EMA, given that the ICH guidelines are implemented by the EMA and treated like EMA-originating guidelines.

#### 4. TRANSPARENCY – ENHANCING PARTICIPATION AND ACCOUNTABILITY

Transparent decision-making processes are imperative to the exercise of public control.<sup>125</sup> Transparency is a prerequisite for citizens to be able to understand government action and to facilitate meaningful contestation.<sup>126</sup> However, although transparency is deemed to be a very important component and in fact a prerequisite of legitimate decision-making, it should not easily be assumed that transparency leads to democratic legitimacy. It should rather be regarded as a starting point for the participation of civil society and democratic control.<sup>127</sup> It can be achieved through a variety of mechanisms, encompassing clear information about decision-making processes and the topic subject to debate, access to documents, reason giving as well as information on who is participating in a decision-making process.<sup>128</sup> Such transparency mechanisms can be used passively by providing the information only where this is requested, or actively through providing information without prior request, for example on the website of the respective institution.<sup>129</sup>

##### 4.1 *Assessing ICH transparency*

In the early years of the ICH procedure and especially before the rise of the internet, information on the ICH and its procedures was very sparse. In his article from 1995, Contrera sees a weakness in the ICH regulatory process in its transparency. At this time the only possibility of obtaining information on the harmonisation activities were the public consultations, through the national/regional authorities during the third step of the ICH process.<sup>130</sup> He suggested that the ICH was keeping the public uninformed about its activities, based on the rather dated view of the patient being better kept uninformed in health matters, leaving their regulation to the experts.<sup>131</sup>

However, a lot has changed in the past 20 years and the approach to transparency within the ICH has changed at least partially. With regard to the ICH Reform, the Press Release announcing the organisational changes stated that: '(t)he reforms strengthen ICH as the leading platform for global pharmaceutical regulatory harmonisation, and one that brings

<sup>125</sup> R. Grant & R. Keohane, 'Accountability and Abuses of Power in World Politics', 99(1) *American Political Science Review* (2005), pp. 29-43, p. 39.

<sup>126</sup> P. Craig, *EU Administrative Law* (Oxford: Oxford University Press, 2012), p. 356f.

<sup>127</sup> Curtin & Meijer (2006), p. 120; Möllers (2006), p. 319.

<sup>128</sup> Alemanno (2014), p. 82.

<sup>129</sup> Curtin & Meijer (2006), p. 113; Alemanno (2014), p. 75ff.

<sup>130</sup> Contrera (1994-1995), p. 956.

<sup>131</sup> *Ibidem*.

together *in a transparent manner* all key regulatory authorities and industry stakeholders.<sup>132</sup>

Nowadays the main publication tool and source of information is the website which is run by the ICH secretariat.<sup>133</sup> Any interested member of the public can find information on ICH history,<sup>134</sup> membership,<sup>135</sup> as well as the ICH's founding documents in the form of Articles of Association and the Rules of Procedure of the bodies.<sup>136</sup> Moreover, information on the core of the ICH work, the guidelines as a final result of the standard-setting process, are made accessible to the public.<sup>137</sup> For the guidelines which have reached step 5 in the procedure, leading to implementation in the national or regional pharmaceutical regulation, the website provides the source of the measure through which the guideline is implemented, currently at least for the Founding Regulatory Members and the Standing Regulatory Members.

Overall, the transparency of the ongoing ICH activities has increased. The Steering Committee Meeting Reports have been published since 2005. However, in the course of the reform process they have been removed from the website. Since the reform, the ICH has been publishing the minutes of the Management Committee meetings and summary reports of teleconferences,<sup>138</sup> as well as agenda papers and minutes of the Assembly meetings.<sup>139</sup> In this regard, the Rules of Procedure of the Assembly state that the minutes of the Assembly meetings, which are made available on the ICH website, will not only provide a summary record of the discussion, but may also contain information on possible dissenting views.<sup>140</sup> Especially if decisions are not taken by consensus, but the Assembly proceeds to vote, the minutes will indicate how the individual members voted and should reflect the discussion that has taken place.<sup>141</sup> This would indeed increase the transparency of the decision-making, at least with regard to the selection of guidelines topics and the adoption of final guidelines.

Additionally, the transparency of the ICH process has been increased through the current reform as the ICH now also publishes an annual report as well as yearly work plans and multi-annual strategic plans.<sup>142</sup> The annual report provides an overview of the main activities of the association and its respective bodies, including the key decision of the Assembly and the Management Committee, as well as an overview of all ICH Working Groups and the anticipated next steps in the decision-making process of the guidelines they are preparing.<sup>143</sup> The annual work plan is adopted in table format and is categorised to cover harmonisation, procedures, strategy, and operations, providing for the activity that has to be

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<sup>132</sup> ICH, Press Release – ICH announces organisational changes as it marks 25 years of successful harmonisation, Geneva, 26 October 2015 (emphasis added).

<sup>133</sup> <http://www.ich.org>, last accessed: 3 April 2017.

<sup>134</sup> <http://www.ich.org/about/history.html>, last accessed: 3 April 2017.

<sup>135</sup> <http://www.ich.org/about/membership.html>, last accessed: 3 April 2017.

<sup>136</sup> <http://www.ich.org/about/articles-procedures.html>, last accessed: 3 April 2017.

<sup>137</sup> <http://www.ich.org/products/guidelines.html>, last accessed: 3 April 2017.

<sup>138</sup> <http://www.ich.org/meetings/management-committee.html>, last accessed: 3 April 2017.

<sup>139</sup> <http://www.ich.org/meetings/assemblyreports.html>, last accessed: 3 April 2017.

<sup>140</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 17.

<sup>141</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 17.

<sup>142</sup> To be accessed via: <http://www.ich.org/about/work-plans-reports.html>, last accessed: 3 April 2017.

<sup>143</sup> ICH, ICH Association 2015 Annual Report, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Work\\_plans\\_Reports/2015\\_Annual\\_Report\\_ICH\\_Association\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Work_plans_Reports/2015_Annual_Report_ICH_Association_Final.pdf), last accessed: 3 April 2017.

undertaken in the respective category, which body is responsible, and the anticipated timeline.<sup>144</sup> For example, the work plan for 2017 under the category strategy provides that the ICH will develop a transparency policy for which the Management Committee will be responsible. However, no further detail on the transparency policy is provided.<sup>145</sup> The multi-annual strategic plan contains harmonisation, communication, procedures and operations activities for the following five years, albeit in a very general and abstracted way.<sup>146</sup> These documents certainly improve the transparency of the overall development of the ICH as an organisation, but more so in general governance terms. It remains to be seen whether the planned transparency policy will introduce further novelties with regard to making the ICH process more transparent.

Nonetheless, one of the main traits of transparency is to make public who has taken part in the decision-making process. As discussed, the membership of the Working Parties remains opaque.<sup>147</sup> This constitutes a transparency problem as industry involvement in the guideline drafting process cannot be traced. According to an EFPIA representative, the publication of names of experts in the working groups was discussed, but abandoned due to concerns regarding the publication of personal data.<sup>148</sup>

Although the transparency of the ICH has increased generally and importantly, the guidelines as end products of the harmonisation process are accessible, what persists is a lack of ‘decisional transparency’ in the guideline drafting process.<sup>149</sup> The consensus forming process in the Expert Working Groups remains opaque and no information is available which could give more indications as to how the scientific consensus was reached and which arguments were discussed. The Work Groups according to the Standard Operating Procedures will now publish work plans.<sup>150</sup> However these plans document when meetings of teleconferences will take place and when a guideline should reach the next step of the procedure, but no information on the substance of the guideline and the ongoing discussion is provided.<sup>151</sup>

As pointed out in the section addressing participation in the ICH, a transparency problem also exists with regard to the public consultation procedure.<sup>152</sup> While public consultations are easily accessible, the biggest transparency lacuna is the omission of publication of the comments received by the regulatory members and the ICH, or summaries thereof, and reasons why they have or have not been taken into account. Publication of these comments would contribute to a better understanding of the consensus formed and would also give the ICH the opportunity to give reasons for its decisions,

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<sup>144</sup> ICH, ICH Association 2017 Annual Work Plan, 10 November 2016, MC 2016/40, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Work\\_plans\\_Reports/-ICH\\_Association\\_Work\\_Plan\\_2017\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Work_plans_Reports/-ICH_Association_Work_Plan_2017_Final.pdf), last accessed: 3 April 2017.

<sup>145</sup> ICH, ICH Association 2017 Annual Work Plan, 10 November 2016, MC 2016/40, p. 3.

<sup>146</sup> ICH, ICH Association Multi-Annual Strategic Plan, 10 November 2016, MC 2016/40, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Work\\_plans\\_Reports/-ICH\\_Association\\_Multi-Annual\\_Strategic\\_Plan\\_Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Work_plans_Reports/-ICH_Association_Multi-Annual_Strategic_Plan_Nov2016.pdf), last accessed: 3 April 2017.

<sup>147</sup> Section 3.

<sup>148</sup> Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author.

<sup>149</sup> See also: Dagron (2012), p. 19.

<sup>150</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, p. 17.

<sup>151</sup> See for example: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/-Guidelines/Safety/S1/S1\\_EWG\\_Work\\_Plan\\_9Aug2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/-Guidelines/Safety/S1/S1_EWG_Work_Plan_9Aug2016.pdf), last accessed: 3 April 2017.

<sup>152</sup> Section 2.

ultimately increasing the legitimacy of the standards. In addition, the fact that comments or summaries are not published, also conceals who has taken the opportunity to actually comment via this procedure. According to an interview carried out with EMA officials, the parties providing comments vary greatly depending on the topic both with regard to ICH guidelines and EMA originating guidelines. The main respondents are usually from industry, as well as healthcare professionals or patients' organisations, as well as other interest groups.<sup>153</sup> With regard to the public consultations the US FDA carries out for the ICH guidelines, Berman comes to the conclusion that, mainly, the industry participates in the consultations, accounting for the large majority of comments.<sup>154</sup>

Besides publishing information on the website, the ICH also uses meetings to make its activities known. It holds the so-called ICH Public Events as an initiative to increase transparency in the ICH process and to inform non-members about the ongoing proceedings.<sup>155</sup> While they are regularly conducted each year in Japan, they are more sporadic in the US and in Europe, as in the EU such events have only taken place in Europe in 2008, 2014, 2015 and 2016. In Europe they are open to the public, but in 2008 and 2014 have been subject to a fee.<sup>156</sup> At the 2014 Europe meeting organised by the EFPIA together with another professionals' organisation, the participation fees amounted to 880 euros for industry members or 505 euros for academics, government or nonprofit employees.<sup>157</sup> Given these considerable amounts, the ICH Public Events were thus not addressed to the public at large but rather to very specialised persons, being a transparency tool more in the epistemic than in a democratic sense. In 2015 and 2016, however, academics, government and nonprofit employees were exempted from the fee.<sup>158</sup> When it comes to the publication of background information on the meetings, the level of transparency is clearly dependent on the region where the meeting has taken place. The Japanese symposia are either summarised in a report, containing information on organisers, the programme and the presentations, or the presentations are made available (although in Japanese). The information available with regard to the EU and US regional meetings are rather scarce, consisting of the programme only. In this regard, a consistent policy with regard to the transparency of the Public Meeting documents is lacking.

Therefore, the overall picture on transparency of the ICH is mixed. While the importance of transparency and communication to the public for the legitimacy of standard-setting appears to be recognised by the ICH members, there are still flaws with regard to making information available that would facilitate the comprehension of the decision-making process, and would provide an insight into the scientific debate undertaken in the standard-

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<sup>153</sup> Interview with two officials of the European Medicines Agency, conducted in London on 23 March 2015, notes on file with the author.

<sup>154</sup> A. Berman, 'The Role of Domestic Administrative Law in the Accountability of Transnational Regulatory Networks', (2011b) CTEI Working Paper, CTEI-2011-08, p. 16f.

<sup>155</sup> <http://www.ich.org/meetings/ich-public-events.html>, last accessed: 3 April 2017.

<sup>156</sup> [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/E-ICH\\_Public\\_Meetings/-Brussels\\_Belgium\\_14\\_November\\_2008/Brussels\\_Belgium\\_14\\_November\\_2008\\_-\\_Programme.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/E-ICH_Public_Meetings/-Brussels_Belgium_14_November_2008/Brussels_Belgium_14_November_2008_-_Programme.pdf), last accessed: 3 April 2017; [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/E-ICH\\_Public\\_Meetings/2014/DIA\\_Info\\_-\\_Day\\_ICH\\_programme.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/E-ICH_Public_Meetings/2014/DIA_Info_-_Day_ICH_programme.pdf), last accessed: 3 April 2017.

<sup>157</sup> [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/E-ICH\\_Public\\_Meetings/-2014/DIA\\_Info\\_Day\\_ICH\\_programme.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/E-ICH_Public_Meetings/-2014/DIA_Info_Day_ICH_programme.pdf), last accessed: 3 April 2017.

<sup>158</sup> [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/E-ICH\\_Public\\_Meetings/2015/-Info\\_Day\\_on\\_ICH\\_DIA\\_April\\_2015.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/E-ICH_Public_Meetings/2015/-Info_Day_on_ICH_DIA_April_2015.pdf); [http://www.ich.org/fileadmin/Public\\_Web\\_Site/-Meetings/E-ICH\\_Public\\_Meetings/2016/DIA\\_Training\\_in\\_Germany\\_6Apr2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/-Meetings/E-ICH_Public_Meetings/2016/DIA_Training_in_Germany_6Apr2016.pdf), last accessed: 3 April 2017.

setting process. These transparency flaws are amplified, as they need to be evaluated in combination with the imbalanced participation and lack of conflict of interest procedures identified in the previous sections.

#### 4.2 *EU perspective: EMA and the principle of transparency*

As discussed in Chapter 2, transparency forming part of the principle of openness in the EU is regarded as a central democratic value.<sup>159</sup> According to Article 1 TEU the Union is committed to take ‘decisions (...) as openly as possible’. In Article 15 TFEU it is specified that ‘institutions, bodies, offices and agencies shall conduct their work as openly as possible’ to foster good governance and facilitate participation. It is, furthermore, also specifically demanded from the European administration through Article 298 TFEU. This transparency commitment is to be understood to relate to access to documents (Article 15(3) TFEU, Article 42 Charter), which is specified in the access to document Regulation 1049/2001 (EC) as a right for every Union citizen, as well as legal or natural persons which reside in the Union or have a registered office there, subject to certain procedures and conditions.<sup>160</sup> The Regulation is not directly applicable to agencies as such, but has been made applicable to the EMA in its founding regulation.<sup>161</sup> However, the transparency commitment of the Union extends beyond the passive provision of information upon request, to include active duty to open up the decision-making processes in the EU as provided for in Article 15(1) TFEU.

Again, in order to specifically define the content of the principle of openness, the policy that the respective EU body has established, must be looked at, since no overall framework applies. The European Medicines Agency has been subject to Ombudsman criticism with regard to its transparency in a case from 2010, concerning an access to documents request.<sup>162</sup> However, since then it has ‘substantially broadened’<sup>163</sup> its transparency policy. In its ‘Road map to 2015’ it has committed to increasing its transparency, also working on the means for providing information and how to convey the highly scientific and technical content of its activities.<sup>164</sup> The main transparency mechanism for the active provision of information with regard to the EMA is its website which provides information on the mandate and work of the agency as well as a search option to get information on specific medicines. The website provides extensive information and is directed not only to industry and other experts, but also makes an effort to address the general public. It provides information on the agency structure and introduces the staff working in the higher

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<sup>159</sup> Chapter 2, Section 5.2. For a good overview of the principle of transparency in the EU see: Craig (2012), pp. 356-366.

<sup>160</sup> Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31 May 2001, pp. 43-48.

<sup>161</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 73.

<sup>162</sup> European Ombudsman, Decision of the European Ombudsman closing her inquiry into complaint 1877/2010/FOR against the European Medicines Agency, 2 December 2013.

<sup>163</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 45; See also: European Ombudsman, Ombudsman applauds European Medicines Agency’s new transparency policy, Press Release No. 22/210, 01 December 2010, available via: <http://www.ombudsman.europa.eu/en/press/release.faces/en/5498/html.bookmark>, last accessed: 3 April 2017.

<sup>164</sup> EMA, Road map to 2015 – The European Medicines Agency’s contribution to science, medicines and health, Adopted by the Agency’s Management Board on 16 December 2010, p. 11.

management level, also providing access to their declarations of interest.<sup>165</sup> Importantly, the membership of the CHMP and other scientific committees, including the declarations of interest for these members, is made accessible via the website.<sup>166</sup> In order to provide more insight into the work of the CHMP, the agendas of the meetings as well as minutes of the meeting are made available.

However, although the discussion and adoption of guidelines does form part of the CHMP meeting agenda, the information is kept to organisational matters stating the name of the guideline and whether it is tabled for information or adoption without going into detail on the substance of discussion.<sup>167</sup> Similarly, where guidelines are prepared in Working Parties, the members of the Working Parties are known, but the information that is provided in the work plans of such Working Parties is rather abstract.<sup>168</sup> Thus like the ICH the information provided by agendas, meeting minutes and work plans does not go beyond the information that a guideline was worked on or adopted. However, unlike the ICH, the membership of the organs involved in the drafting process is known. Through the public list of European experts, the conflict of interest declarations as well as the CVs of the experts involved in the guidelines drafting process are accessible.<sup>169</sup>

The question whether transparency with regard to the experts involved in the drafting of guidance documents by an Agency could conflict with the protection of personal data of the respective experts, the Court of Justice in a case involving the European Food Safety Authority (EFSA) has taken a firm position to the benefit of transparency.<sup>170</sup> In the *ClientEarth* case, the Court confirmed that in order to be able to challenge the choice of experts in terms of partiality, the NGOs that had filed a request for access to documents could not only obtain access to the names, declarations of interests and CVs of the experts involved, but would also be entitled to obtain information that would allow them to identify which expert made which comment in the guideline drafting procedure.<sup>171</sup> EFSA's argument that this could lead to individual attacks on the experts, according to the Court, cannot be used as an argument to deny the access to the respective information without specific evidence.<sup>172</sup>

With regard to the EMA's scientific guidelines, the homepage has one section specifically devoted to 'scientific guidelines' introducing the tasks of the agency and

<sup>165</sup> See: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/general/general\\_content\\_000112.jsp&mid=WC0b01ac0580028a43](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000112.jsp&mid=WC0b01ac0580028a43), last accessed: 3 April 2017.

<sup>166</sup> For the CHMP membership and declarations of interest see: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/general/general\\_content\\_000094.jsp&mid=WC0b01ac0580028c79](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000094.jsp&mid=WC0b01ac0580028c79), last accessed: 3 April 2017.

<sup>167</sup> The CHMP agendas are available via: [http://www.ema.europa.eu/ema/-index.jsp?curl=pages/about\\_us/document\\_listing/document\\_listing\\_000378.jsp&mid=WC0b01ac0580028d2a](http://www.ema.europa.eu/ema/-index.jsp?curl=pages/about_us/document_listing/document_listing_000378.jsp&mid=WC0b01ac0580028d2a), last accessed: 3 April 2017.

<sup>168</sup> The work plans for CHMP working parties are available via: [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/general/general\\_content\\_000102.jsp&mid=WC0b01ac058002d0ec](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000102.jsp&mid=WC0b01ac058002d0ec), last accessed: 3 April 2017.

<sup>169</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/landing/experts.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/experts.jsp), last accessed: 3 April 2017.

<sup>170</sup> Case C-615/13P *ClientEarth and Pesticide Action Network Europe (PAN Europe) v. European Food Safety Authority*, ECLI:EU:C:2015:489.

<sup>171</sup> Case C-615/13P *ClientEarth and Pesticide Action Network Europe (PAN Europe) v. European Food Safety Authority*. ECLI:EU:C:2015:489, para. 60.

<sup>172</sup> Case C-615/13P *ClientEarth and Pesticide Action Network Europe (PAN Europe) v. European Food Safety Authority*, ECLI:EU:C:2015:489, paras. 65-70.

providing access to the procedure for the adoption of guidelines.<sup>173</sup> There, the EMA publishes the finalised, adopted guidelines on its website and even has a specific section for guidelines originating in the ICH. Moreover, according to the procedure that has been in force since September 2005, during the guidelines drafting process, the respective guideline concept paper and draft are published and subject to a consultation procedure.<sup>174</sup> Thus, the internal process of finding scientific consensus will become visible at two occasions before the adoption of the final guideline.<sup>175</sup> Additionally, according to the agency's guideline drafting procedure, the comments received in the consultation procedure will be published on the website, except where the author of the comment has denied the publication or where commercially confidential information is part of the comment.<sup>176</sup> These comments are furthermore synthesised into a document that points out the main comments and explains the agencies' position on them.<sup>177</sup> Therefore, with regard to the 'decisional transparency', the EMA procedure provides significant advantages in transparency of the procedure, leading to the adoption of a guideline.

### 4.3 *Uploading EU administrative law: transparency*

Overall, it has to be concluded once again that the EMA's approach to transparency in the guideline drafting process provides significant advantages over the transparency in the ICH process. The procedural standards in the EU with regard to transparency are at a higher level than at the ICH. Although the EMA guideline drafting process does not have institutionalised industry involvement, it is additionally ensured that the interests of the participating members of the scientific Committees are transparent.

Therefore, what can be learned from the EMA guideline drafting procedure, and the transparency requirements, with regard to consulted scientific experts in the EU in general is as follows: it is inherent for the legitimacy of a scientific guideline to know who has taken part in the decision-making process; in particular, how private interests might have influenced the opinions voiced by respective experts. Apart from transparency about who is consulted, the scientific discussion itself becomes more transparent in two key ways: through the publication of drafts in two steps of the public consultation process, and through the publication of comments, together with reasoning on how they were integrated into the draft or why they were not.

## 5. CONCLUSION

The logic invoked for the creation of global standard-setting bodies, and the increasing involvement of private parties, is the complexity of risk faced in society today, and the expertise required to address this. Indeed, the expertise represented in the respective

<sup>173</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/-general\\_content\\_000043.jsp&mid=WC0b01ac05800240cb](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/-general_content_000043.jsp&mid=WC0b01ac05800240cb), last accessed: 3 April 2017.

<sup>174</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 11.

<sup>175</sup> Section 2.

<sup>176</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 13.

<sup>177</sup> European Medicines Agency, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009, p. 13.

regulatory industry often offers the industry a favourable position over other stakeholders in global governance structures. There is a danger of turning governance based forms of risk regulation into ‘bureaucratic micromanagement’, which cannot be reconciled with democracy.<sup>178</sup>

The close analysis of the procedural standards conducted in this chapter – with regard to participation, independent expertise, and transparency – has shown that there are still flaws in the ICH's practical application of the assessed principles. This is despite the fact that, like other global bodies, the ICH is increasingly trying to improve its procedural legitimacy still flaws with regard to practical application of the assessed principles remain. In terms of participation, the ICH retains a heavy industry bias whilst largely excluding the representation of other interests in the decision-making procedure. It is highly questionable whether such an institutional set-up can really live up to the mandate of protecting public health. This structural problem of the institutionalisation of industry interests is aggravated by the lack of independent expertise, which could be remedied through a conflict of interest policy. Moreover, a recurring problem in the discussion of the ICH decision-making process is the lack of decisional transparency, as public control cannot be exerted on the forming of scientific consensus.

This chapter has argued that procedural norms can be ‘uploaded’ from EU administrative law, especially with the principles of participation, independent expertise and transparency. Concerning stakeholder participation, the institutional structures and procedural rules supporting weaker stakeholders as used by the EMA could provide inspiration for the ICH decision-making process. Regarding the principle of independent expertise, it was shown that as a public-private partnership the ICH is as such irreconcilable with the requirement of independent expertise applicable to administrative activities in the EU. What could be transposed to the global level, however, are conflict of interest policies that make potential and existing conflicts of interest visible. Finally, a gap in the decisional transparency of the ICH was identified. The transparency of the EMA committees and other scientific bodies could serve as inspiration for the ICH, and could contribute to forming a norm for decisional transparency in international administrative law.

It was established in this research that, regardless of the procedural flaws identified, once they are implemented into the EU regulatory framework the ICH guidelines have the same status as other EMA guidelines. Thus, the procedural standards applicable in the EU, which are consistently not lived up to in the ICH process, are bypassed through the outsourcing of standard-setting to the global level. This creates a two-tier system of procedural protection in the guideline drafting process, creating a distinction between the different origins of a guideline, whereas the *de facto* effects of these guidelines on the institutions, Member States, natural as well as legal persons remains the same.

The analysis of the ICH's institutional structure and procedure shares the same characteristics as the EU's risk regulation in the food safety area prior to the BSE crisis: with an industry-focused regulatory body operating under conditions of secrecy and advice given in small closed groups of experts.<sup>179</sup> In essence, the ICH standard-setting is the epitome of a mode of governance that the EU has aimed to overcome for the sake of good governance since the beginning of this millennium.<sup>180</sup> It is remarkable that while the EU increasingly

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<sup>178</sup> Shapiro (2001), p. 373.

<sup>179</sup> E. Millstone & P. van Zwanenberg, ‘The Evolution of Food Safety Policy-Making Institutions in the UK, EU and Codex Alimentarius’, 36(6) *Social Policy & Administration* (2002), pp. 593-609, p. 593.

<sup>180</sup> European Commission, European Governance – A White Paper, COM(2001) 428 final, OJ 287 12.10.2001, pp. 1-29.

aims at improving the legitimacy of its own decision-making by means of increased transparency and participation, global standards are absorbed into the legal framework of the European Union without being measured against the same benchmarks of good governance. This finding is highly problematic as it shows that existing good governance requirements can be circumvented through the ‘outsourcing’ of regulatory power to the global level. Therefore, the research shows that a discussion on increasing the transparency, participation and independence of European agencies is incomplete as long as it falls short in paying attention to what happens beyond the EU level.

## Chapter 7: Global pharmaceutical standards as challenge for EU Law – remedies within the EU

### 1. INTRODUCTION

The previous chapter analysed the legitimacy of the ICH standard-setting procedure by applying the perspective of EU administrative law. This has led to the identification of several gaps and proposals on how the ‘upload’ of European procedural standards could benefit the ICH standard-setting procedure and institutional structure. The ICH structure as a public-private partnership introduces a heavy industry bias that is not balanced by the participation of other stakeholders. Moreover, the industry bias is not controlled in any form through a conflict of interest policy, and important parts of the operation of the ICH remain opaque.

The EU implements ICH standards in a regulatory system where they significantly influence pharmaceutical regulation, as shown in Chapter 5. However, this also implies significant problems for the EU as an implementing system, where the global standards it receives are ‘hollowing out’<sup>1</sup> procedural rules applicable to the same type of guidance documents on the European level. This is all whilst assigning the implemented global standards with the same legal value as the ones adopted in a European procedure.

The previous chapter examined whether the uploading of EU administrative law norms and procedures would contribute to improving the ICH institutional structure and decision-making process. This chapter is concerned with questioning if the legitimacy gaps that are identified can be mitigated on the European level. The chapter will address whether existing accountability mechanisms within the EU could mitigate the legitimacy gaps of the implemented ICH guidelines as part of the EU regulatory framework for pharmaceuticals. Political accountability (Section 2) and judicial accountability (Section 3) will be distinguished. Moreover, it will examine juridification as a potential remedy, distinguishing between introducing ex-ante and ex-post procedures with regard to the implementation of global standards in the EU (Section 4.1) and juridification in an EU administrative procedure act (Section 4.2).

### 2. POLITICAL ACCOUNTABILITY WITHIN THE EU FOR GLOBAL PHARMACEUTICAL STANDARDS – A REMEDY WITH LIMITS

As explained in Chapter 2, accountability as understood in this research is not to be equated with legitimacy, but forms one of the factors that contributes to legitimate regulation.<sup>2</sup> It was also pointed out that with regard to the accountability of bodies on the international or global level, many of the accountability mechanisms applied to regulators in national systems will not apply equivalently. This section however is not concerned with ICH accountability for the standards that it sets on the global level, but it is focused on the accountability within the EU of the EU actors that take part in the ICH process, and that are responsible for the implementation of ICH standards in the EU.

The approach taken is to examine ICH accountability for its standard-setting from a European perspective, in conjunction with the overall focus of this research. The focus is on the European actors participating in the process and implementing the guidelines. In this regard, it of course also needs to be acknowledged that this section only studies EU accountability mechanisms while the ICH membership is broader. Therefore, the domestic

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<sup>1</sup> Mendes (2012), pp. 988-1022.

<sup>2</sup> Chapter 2, Section 2.2.

accountability of other ICH members might also contribute to the enhanced legitimacy of the ICH. Further research is required to identify the effect of the interaction of the different accountability regimes on the global level, and within the ICH member states and regions on the accountability of the ICH.<sup>3</sup>

As the implementation of the ICH guidelines in the EU is executed through the adoption of an EMA guideline, from a procedural perspective only the Commission and the EMA are contributing to the content of the guidelines on the global level and their implementation into the EU regulatory framework. No other EU institution or body plays a role in the implementation of the ICH guidelines or would exercise any procedural control in the implementation of these guidelines. Therefore, this chapter will examine whether *ex post* political accountability mechanisms at the European level are applicable to the Commission and the EMA, with regard to the reception of ICH standards in the EU.

Thus, accountability of the European actors within the ICH can be one legitimating factor. It might counterbalance legitimacy flaws identified in the ICH process. To provide an example: one could argue that through the accountability of the Commission and EMA for the implementation of ICH standards towards the European Parliament, the democratic legitimacy of the reception of ICH standards in the EU regulatory framework would be enhanced. Nonetheless it needs to be acknowledged that political accountability itself is subject to certain limitations. In the example chosen, one for instance also needs to acknowledge the legitimacy challenges the European Parliament is facing itself.<sup>4</sup> Moreover, empirical research would be required to identify whether parliamentary accountability would indeed contribute to counterbalancing the industry participation in the ICH and the lack of access of other stakeholders to the ICH process. Thus, while an assessment of the accountability of the European actors for their ICH involvement should be examined, this accountability within the EU does not necessarily fully remedy the legitimacy flaws of the ICH process on the global level.

In the following, referring to accountability as a relationship consisting of information, questioning, judging and sanctioning stages,<sup>5</sup> it will be examined whether other EU institutions are informed about the standard-setting in the ICH process, and if they could interfere and eventually mitigate the legitimacy gaps that have been identified in this research.<sup>6</sup>

### 2.1 *Reporting obligations of the Commission and the European Medicines Agency*

First of all, the basis for accountability is the provision of information and in this regard, both the European Commission and the European Medicines Agency, as a proceduralized reporting obligation, publish annual activity reports.

With regard to the European Commission, the annual activity reports adopted by DG SANTE could function as a source of information on the Commission's activities in the ICH. According to Curtin, these reports are however more an internal accountability

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<sup>3</sup> Berman has assessed the accountability mechanisms for the US participation in the ICH. See: Berman (2011b), p. 16.

<sup>4</sup> See prominently: J. Weiler, U. Haltern & F. Mayer, 'European Democracy and its Critique', 18(4) *West European Politics* (1995), pp. 4-39.

<sup>5</sup> Bovens (2007), p. 450.

<sup>6</sup> Further analysis of the accountability of the EU executive as well as the Commission and European agencies is provided by: Curtin (2009); M. Busuioc, *European Agencies: Law and Practice of Accountability* (Oxford: Oxford University Press, 2013); M. Scholten, *The Political Accountability of EU and US Independent Regulatory Agencies* (Leiden: Brill Nijhoff, 2014).

mechanism geared at providing an account of administrative and managerial issues.<sup>7</sup> Nonetheless, the 2015 DG SANTE activity report does mention the ICH:

‘DG SANTE continued to promote EU norms in multilateral and bilateral trade agreements to maintain high health standards and reduce costs for exporters. The reorganisation of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was finalised. This will increase the participation of key partners and promote the recognition of ICH guidelines as international standards.’<sup>8</sup>

However, there are no indications of DG SANTE’s involvement in the ICH in the 2013 and 2014 annual reports.<sup>9</sup> Arguably, the statement above does not provide much detail on EU involvement in the ICH and the effect of ICH guidelines on the regulatory framework of the EU.

The EMA is subject to an obligation to submit annual reports on its activities to the European Parliament, the Council, the Commission, the Economic and Social Committee, the Court of Auditors, and the Member States.<sup>10</sup> Moreover, the EMA will also draft an annual work programme which is forwarded to the European Parliament, the Council, the Commission, and the Member States.<sup>11</sup> These reports and work programmes are available on the website of the Agency.<sup>12</sup>

The EMA work programmes over the last years mention the ICH amongst other international organisations and forums with which the EMA collaborates.<sup>13</sup> In 2016 there also was an additional paragraph on the ICH reform.<sup>14</sup> Sometimes specific ICH activities are mentioned; for example the work programme for 2016 lists ‘Promote application of harmonised international standards’ as an objective for the EMA under ‘Additional objectives and activities’. There is an objective to ‘Provide technical and scientific contribution to the development of an addendum to the ICH statistical principles guideline E9 and of an addendum to the ICH Paediatrics guideline E11, relating to the design and

<sup>7</sup> Curtin (2009), p. 257.

<sup>8</sup> European Commission, 2015 Annual Activity Report Directorate General for Health and Food Safety, Ref. Ares(2016)1611103 – 05/04/2016, p.9, available via: [https://ec.europa.eu/info/sites/info/files/activity-report-2015-dg-sante\\_april2016\\_en.pdf](https://ec.europa.eu/info/sites/info/files/activity-report-2015-dg-sante_april2016_en.pdf), last accessed: 3 April 2017.

<sup>9</sup> European Commission, 2014 Annual Activity Report Directorate General for Health and Consumers, available via: [https://ec.europa.eu/info/publications/annual-activity-report-2014-health-and-consumers\\_en](https://ec.europa.eu/info/publications/annual-activity-report-2014-health-and-consumers_en), last accessed: 3 April 2017; European Commission, 2013 Annual Activity Report Directorate General for Health and Consumers, available via: [https://ec.europa.eu/info/publications/annual-activity-report-2013-health-and-consumers\\_en](https://ec.europa.eu/info/publications/annual-activity-report-2013-health-and-consumers_en), last accessed: 3 April 2017.

<sup>10</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Arts. 64(3) jo. 65(10).

<sup>11</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Arts. 64(3) jo. 65(9).

<sup>12</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/document\\_listing/-document\\_listing\\_000208.jsp&mid=WC0b01ac058002933a](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/document_listing/-document_listing_000208.jsp&mid=WC0b01ac058002933a), last accessed: 3 April 2017.

<sup>13</sup> EMA, Work Programme 2015, 18 December 2014, EMA/773839/2014 Rev. 1, p. 45; EMA, Work Programme 2014, 12 December 2013, EMA/695772/2013, p. 35.

<sup>14</sup> EMA, Work Programme 2016, 5 July 2016, EMA/92499/2016 Rev. 1, p. 48f. On page 49 the work programme states: ‘Reforms to ICH – now called the International Council for Harmonization – will come fully into force in 2016, allowing for a broader global membership and strengthening ICH as the leading platform for global pharmaceutical regulatory harmonisation. The Agency plays an important role in supporting the European Commission by coordinating the EU expertise and contribution to the work of ICH.’

analysis of clinical trials’, as well as: ‘Provide technical and scientific contribution to the development of ICH safety guidelines (Carcinogenicity assessment document evaluation for ICH S9)’.<sup>15</sup> The annual activity reports contain Annexes that list adopted EMA guidelines and include a specific section listing the ICH guidelines as adopted by the EMA.<sup>16</sup> In addition to these reporting obligations, the EMA more recently is also publishing shorter annual reports containing more general information on developments in the Agencies’ activities and infographics. The annual reports for 2014 and 2015 contained a section called ‘International collaboration’ which includes a paragraph on EMA participation in the ICH.<sup>17</sup>

However, whether the work programmes and the annual reports provided by the Commission and the EMA are an effective means to control the activities of the EU executive with regard to its activities in the ICH and the implementation of the ICH standards in the EU is to be doubted. The information in these documents is very general and usually does not extend beyond mentioning that the Commission or the EMA participated in the ICH or in very significant activities such as the ICH reform. It is questionable whether such reports subsequently trigger a closer examination of the Commission and EMA activities through other European institutions such as the Parliament. Empirical research has shown that representatives of the Agencies in general, while acknowledging the relevance of these reports, ‘are generally reluctant to regard it as a powerful instrument of parliamentary accountability’.<sup>18</sup> However, in the following the accountability of the Commission and EMA for their role in the creation and implementation of ICH standards towards relevant European institutions and bodies is evaluated.

## 2.2 *The Council and the European Parliament*

As was explained in Chapter 3, the adoption of scientific guidelines serves to clarify the legislative requirements of quality, safety and efficacy of medicinal products. Therefore, this section will examine whether the Commission and the EMA remain accountable to the Council and the Parliament in their guideline adoption and, therefore, also the implementation of ICH guidelines.

Both the Council and the European Parliament are kept informed about the ICH activities of the Commission and the EMA through the reports and work programmes as indicated before. However, although in-depth empirical research about the accountability relationship of the Council and the Parliament with regard to the ICH involvement of the

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<sup>15</sup> EMA, Work Programme 2016, 5 July 2016, EMA/92499/2016 Rev. 1, p. 26.

<sup>16</sup> EMA, Annexes to the annual report of the European Medicines Agency 2015, p. 57f, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Annual\\_report/2016/05/WC500206481.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2016/05/WC500206481.pdf), last accessed: 3 April 2017.

<sup>17</sup> EMA, Annual Report 2015, p. 31f, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Annual\\_report/2016/05/WC500206482.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2016/05/WC500206482.pdf), last accessed: 3 April 2017; EMA, Annual Report 2014, p. 15, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Annual\\_report/2015/04/WC500186306.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2015/04/WC500186306.pdf), last accessed: 3 April 2017. The 2015 Annual Report states: ‘The International Council on Harmonisation (ICH), (formerly the International Conference on Harmonisation), is the longest standing international forum in which the Agency participates. The ICH underwent major structural and organisational reforms in 2015 with its establishment as a legal entity, a non-profit international association under Swiss law, of which the European Commission is a founding member. EMA contributed to this reorganisation and the Agency will continue to participate in the ICH by providing scientific and technical support to the Commission, including coordinating the participation of experts from the network.’

<sup>18</sup> Busuioc (2013), p. 119.

Commission and EMA is lacking, this research has not identified any occasion where the Council or the Parliament would have interfered with the activities of the Commission and the EMA.

It should be mentioned that the Commission with regard to the reform of the ICH has informed the Council Working Party on Pharmaceuticals and Medical Devices.<sup>19</sup> However, it is not clear from the agenda documents if the Working Party also provided input or whether it was simply informed. Notably, these were the only instances found in the Council's document database in which ICH matters were discussed in the Council.<sup>20</sup> The fact that the interaction between the EU executive and the ICH is only discussed in Council where major changes in the ICH are taking place, indicates that the Council is a rather weak accountability forum. No accountability relationship between the EMA and the Council regarding its ICH tasks appears to be in place. This seems to be in accordance with the conclusion drawn by the general research carried out on the accountability of EU agencies, showing that the Council in general is not keen on holding agencies to account.<sup>21</sup> As far as the day-to-day implementation of ICH guidelines is carried out by the EMA, this process seems to fall under the Council's radar.

Still, especially through the EU budget procedure, both the Council and the Parliament would have the possibility of acting as an accountability forum.<sup>22</sup> Especially given that the ICH will now be membership financed, and therefore the Commission will have to pay a membership fee for participation in the ICH, the budgetary procedure might prove to be a viable route for the Council and the Parliament to hold the EU representatives in the ICH accountable.<sup>23</sup>

Indeed, the European Parliament has in the course of time increasingly acted as an accountability forum for the Commission and also the European agencies.<sup>24</sup> The European Parliament appoints the Commission,<sup>25</sup> and may ask questions to the Commission and organise debates with the Commission.<sup>26</sup> In addition, the annual report of the Commission is discussed in Parliament.<sup>27</sup> Moreover, any Member of the European Parliament can ask written questions to the Commission, which has to reply in writing.<sup>28</sup>

As far as the European agencies are concerned, in the past the Parliament used to omit a detailed discussion of the annual reports or questionings of the agency directors, however

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<sup>19</sup> See for example: Council of the European Union – General Secretariat, Notice of Meeting and Provisional Agenda – Working Party on Pharmaceuticals and Medical Devices Friday 19 July 2013, CM 3637/13, available via: <http://data.consilium.europa.eu/doc/document/CM-3637-2013-INIT/en/pdf>, last accessed: 3 April 2017. The agenda item is: 'International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) – Outcome of the discussions on the reform of the ICH at the meeting in La Hulpe, Belgium 1-6 June 2013 – Information from the Commission'.

<sup>20</sup> According to a search of documents in the public register of the Council, <http://www.consilium.europa.eu/register/en/content/int/?typ=ADV>, last accessed: 3 April 2017.

<sup>21</sup> M. Chamon, *European Agencies – Legal and Political Limits to the Transformation of the EU Administration* (Oxford: Oxford University Press, 2016), p. 319.

<sup>22</sup> Art. 314 jo 319 TFEU.

<sup>23</sup> See Chapter 4, Section 2.4.

<sup>24</sup> Curtin (2009), p. 260.

<sup>25</sup> Art. 17(7) TEU.

<sup>26</sup> Art. 230 TFEU; Framework Agreement on relations between the European Parliament and the European Commission, OJ L 204/47, 20.11.2010.

<sup>27</sup> Arts. 233 and 249(2) TFEU.

<sup>28</sup> See: European Parliament, Rules of Procedure, 8th Parliamentary term, July 2014, Rule 130.

it has recently adopted the practice of inviting the directors for hearings.<sup>29</sup> Therefore, the EMA Executive Director will appear regularly before the European Parliament Committee on Environment, Public Health and Food Safety (ENVI).<sup>30</sup> In addition, the founding regulation foresees that prior to the formal appointment of a new EMA Executive Director, the candidate will be heard by the Parliament.<sup>31</sup> Although MEPs do not have the direct right to submit written questions to the agencies, it is possible to address a question for an agency to the Commission, which then forwards the question. However, it will be the Commission that drafts the official written answer, which is also made public, while the response of the Agency remains concealed.<sup>32</sup>

Thus, the European Parliament could indeed function as an accountability forum with regard to the ICH activities of the Commission and the EMA. Nonetheless, currently it does not seem to live up to this function. A search of the Parliament website shows that the ICH was only mentioned in two written questions to the Commission.<sup>33</sup> However, none of these questions directly concerned ICH activities as such or the European participation in the setting of, or implementation of ICH standards, but were concerned with the Falsified Medicines Directive and the use of animal testing for pharmaceutical products.<sup>34</sup>

Should the European Parliament decide to hold EU actors in the ICH accountable, it would have considerable sanctioning power. In conjunction with the growing dialogue between the Commission and the Agencies on the one side, and the Parliament on the other side, one can witness a strengthening in terms of sanctioning power of the Parliament in this accountability relationship. The Parliament's sanctioning power extends to dismissing the Commission as whole,<sup>35</sup> a very harsh sanction, that will unlikely be used to hold the Commission accountable for legitimacy flaws of the ICH standard-setting process. Through an inter-institutional agreement between the Parliament and the Commission, it is possible for the Parliament to request the Commission President to ask a Commissioner to resign.<sup>36</sup> Moreover, the Parliament has to discharge the Commission budget.<sup>37</sup> However, these possibilities are also rather harsh and it is doubtful whether they would be used to hold the Commission accountable for participating in a global standard-setting initiative that does not live up to European procedural standards.

As far as Agencies are concerned, the most important sanctioning tool for the Parliament is the budgetary procedure. And indeed, the Parliament has used its budgetary powers to hold EMA accountable. In the past, the Parliament has used the budgetary

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<sup>29</sup> Curtin (2009), p. 260.

<sup>30</sup> Busuioac (2013), p. 129. See e.g.: European Parliament, Committee on the Environment, Public Health and Food Safety, Draft Agenda Meeting 7 and 8 November 2016, ENVI(2016)1107\_1.

<sup>31</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 64(1). For example, for the re-appointment of the current Executive Director Guido Rasi, the ENVI Committee held a hearing on 13 October 2015. See: European Parliament, Committee on the Environment, Public Health and Food Safety, Draft Agenda Meeting 12 and 13 October 2015, ENVI(2015)1012\_1.

<sup>32</sup> Chamon (2016), p. 322.

<sup>33</sup> According to a search of the European Parliament website, <http://www.europarl.europa.eu/plenary/en/parliamentary-questions.html>, last accessed: 3 April 2017.

<sup>34</sup> European Parliament, Parliamentary Question (E-004699-13), 26 April 2013; European Parliament, Parliamentary Question (E-0561/06), 15 February 2006.

<sup>35</sup> Arts. 17(8) TEU and 234 TFEU.

<sup>36</sup> Framework Agreement on relations between the European Parliament and the European Commission, OJ L 204/47, 20.11.2010.

<sup>37</sup> Art. 329 TFEU.

discharge procedure to address issues beyond the financial management of the EMA,<sup>38</sup> by postponing the discharge to hold the agency accountable for structural problems, such as concerns with regard to the independence of experts.<sup>39</sup> The Parliament also uses the resolutions it adopts in the discharge procedure to criticise the Agency as it did in 2014, asking the EMA to ensure transparency with regard to clinical trials data.<sup>40</sup>

Thus, while both the Council and the Parliament could potentially act as accountability forums with regard to the EU participation in setting ICH standards and their subsequent implementation, they have not yet taken on this role. One hurdle might be the rather sparse information that is provided by the Commission and EMA in their reports. However, it is also questionable whether a seemingly technical process on the global level will attract the attention of the Council and the Parliament.

### 2.3 *Pharmaceutical Committee*

Another European body that has the potential to contribute to the accountability of the activities of the EU administration in the ICH is the Pharmaceutical Committee, which is an advisory Committee to the Commission composed of senior members of the Member States' administrations and which is chaired by the Commission.<sup>41</sup> Consistently, the Commission reports on the progress of ICH guidelines in this committee, and has also discussed the reform of the ICH on several occasions.<sup>42</sup> However, whether this Committee indeed functions as an effective accountability forum has to be questioned, since earlier research has shown that the membership of the Pharmaceuticals Committee overlaps with the membership of the EMA Management Board.<sup>43</sup> Moreover, again in this case it is unclear whether the Committee is only informed or if it provides input and acts as a viable forum of dialogue and contestation. However, further empirical research is needed in order to analyse the role of the Pharmaceutical Committee as an accountability forum for the Commission

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<sup>38</sup> For example in the budgetary discharge procedure for the year 2014, the Parliament asks the Agency to ensure transparency with regard to clinical trials data. See: European Parliament, Resolution of 28 April 2016 with observations forming an integral part of the decision on discharge in respect of the implementation of the budget of the European Medicines Agency for the financial year 2014, (2015/2171(DEC)).

<sup>39</sup> European Parliament, Decision of 25 October 2011 on discharge in respect of the implementation of the budget of the European Medicines Agency for the financial year 2009, (C7-0233/2010 – 2010/2173(DEC)); European Parliament, Decision of 10 May 2012 in Discharge in Respect of the Implementation of the Budget of the European Medicines Agency for the Financial Year 2010, (C7-0281/2011 – 2011/2220 (DEC)).

<sup>40</sup> European Parliament, Resolution of 28 April 2016 with observations forming an integral part of the decision on discharge in respect of the implementation of the budget of the European Medicines Agency for the financial year 2014 (2015/2171(DEC)).

<sup>41</sup> Council Decision 75/320/EEC of 20 May 1975 setting up a pharmaceutical committee, OJ L 147, p. 23.

<sup>42</sup> Information on the meetings of the Pharmaceutical Committee is available via: [https://ec.europa.eu/health/documents/pharmaceutical-committee/human-meeting\\_en](https://ec.europa.eu/health/documents/pharmaceutical-committee/human-meeting_en), last accessed: 3 April 2017. See for example: European Commission, 74th meeting of the Pharmaceutical Committee, 17 March 2015, PHARM 686, Agenda Item 4a International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), Presentation of the European Commission 'ICH Reform State-of-play and next steps', 17 March 2015, available via: <http://ec.europa.eu/health/-files/committee/74meeting/pharm686.pdf>, last accessed: 3 April 2017.

<sup>43</sup> Vos (1999), p. 227.

and also the EMA. In any case, no sanctioning mechanism is available for the Committee to hold the Commission to account with regard to its ICH activities.

#### 2.4 *The Ombudsman and the Court of Auditors*

The European Ombudsman, which is responsible for the investigation of the maladministration of EU bodies, could serve as an accountability forum for the Commission's and EMA's involvement in the ICH.<sup>44</sup> Complaints are possible through every natural or legal person residing or having its registered office in a Member State.<sup>45</sup> Furthermore, the Ombudsman can also act on its own initiative or upon a complaint made by a Member of Parliament.<sup>46</sup> The Ombudsman has held the Commission and the EMA accountable in several instances. The pronounced interest of the Ombudsman in increasing transparency in the field of pharmaceutical regulation has been exemplified by the recent Ombudsman's dialogue with the EMA about the transparency of clinical trials data.<sup>47</sup>

However, the Ombudsman recommendations do not have legal force or binding effect.<sup>48</sup> The process of investigation and the recommendation drafted by the Ombudsman certainly provides a route to deliberation, acting as a less proceduralised accountability forum.<sup>49</sup> Moreover, the Ombudsman reports to the European Parliament about the instances of maladministration identified.<sup>50</sup> Therefore, the Ombudsman seems to be a suitable accountability forum, not for the ICH procedure as such, but to review the EU participation in the ICH as well as the implementation of the ICH standards.

The Commission and the EMA are also subject to budgetary control by the Court of Auditors,<sup>51</sup> which has the task of auditing the EU budget and the expenditure of the bodies, offices and agencies of the European Union.<sup>52</sup> While the Court of Auditors will report to the European Parliament and Council, it has no sanctioning power of its own and a negative statement of the Court of Auditors does not bind the Parliament and Council in the budget procedure.<sup>53</sup> Still, it has the power of naming and shaming, as the reports are published in the Official Journal.<sup>54</sup> However, with regard to the ICH, the Court of Auditors mandate is limited to financial accountability, which thus would only allow a review of the budgetary implications of the EU participation in the ICH. However, the Court of Auditors has already shown its willingness to hold agencies accountable even beyond strictly budgetary issues through drafting a report on the management of conflicts of interest in selected European agencies.<sup>55</sup> Nonetheless, neither the European Ombudsman nor the Court of Auditors have

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<sup>44</sup> Art. 228(1) TFEU, Art. 24 TFEU and Art. 43 Charter of Fundamental Rights (CFR).

<sup>45</sup> Art. 228(1) TFEU, Art. 43 CFR.

<sup>46</sup> Art. 228(1) TFEU.

<sup>47</sup> European Ombudsman, Decision on own-initiative inquiry OI/3/2014/FOR concerning the partial refusal of the European Medicines Agency to give public access to studies related to the approval of a medicinal product, 8 June 2016; European Ombudsman, Decision on own-initiative inquiry OI/3/2014/FOR concerning the partial refusal of the European Medicines Agency to give public access to studies related to the approval of a medicinal product, Press release No. 6/2016, 10 June 2016.

<sup>48</sup> Hofmann, Rowe & Türk (2011), p. 788.

<sup>49</sup> Curtin (2009), p. 271.

<sup>50</sup> Art. 228(1) TFEU.

<sup>51</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 68.

<sup>52</sup> Art. 287 TFEU.

<sup>53</sup> Art. 287 TFEU. For a detailed discussion of administrative accountability to the Court of Auditors see: Hofmann, Rowe & Türk (2011), pp. 728-735.

<sup>54</sup> Art. 287 TFEU.

<sup>55</sup> Vos (2016), p. 222.

served as accountability forum with regard to the EU's involvement in the ICH or the implementation of ICH standards in the EU pharmaceuticals regulatory framework.

### 2.5 *EMA Management Board*

Besides these external accountability mechanisms, the EMA is also subject to an internal accountability system, as the Executive Director is accountable to the EMA Management Board.<sup>56</sup> This Management Board is composed of one representative of each Member State and two representatives each of the Commission and the European Parliament. In addition, the Council, in consultation with the Parliament, appoints two representatives of patients' organisations, as well as representative of a doctors' association and a of a veterinarians' association, based on a list drawn up by the Commission.<sup>57</sup>

As the name suggests, the Management Board serves as an accountability forum for the general management of the agency and not scientific specificities.<sup>58</sup> Thus, while the Management Board could hold the EMA Executive Director accountable for the general policies underlying the EMA's involvement in the ICH, as well as the general system of implementation of ICH guidelines through the EMA, it is not an efficient accountability forum to assess the implementation of specific ICH guidelines. However, the effectiveness of the accountability of European agencies towards their Management Boards also strongly depends on the committed preparation of the members of the Board and the level of information they receive.<sup>59</sup>

There is currently no indication that the Management Board has taken issue with the role of the EMA in the ICH or the implementation of ICH standards. Moreover, the ultimate sanctioning power of the Management Board, the removal of the Executive Director, is dependent on the proposal of the Commission.<sup>60</sup> It also seems to be a rather misplaced sanction, given that the EMA essentially takes part in the ICH on the Commission's request and not based on the decision of its Executive Director.<sup>61</sup>

### 2.6 *A lacuna of political accountability within the EU for implementing global standards?*

The previous analysis has shown that although several European institutions and bodies could function as accountability fora with regard to the participation of the Commission and EMA in the global standard-setting process, and also the implementation of the ICH standards in the EU, in practice these mechanisms are not used to meaningfully hold the respective actors to account. Especially with regard to the Council and the Parliament, which would have the opportunity to be informed and also to exercise sanctioning power, the setting of regulatory standards seems to fall below the radar. This might be explained by the fact that as legislators these bodies have delegated the adoption of pharmaceutical guidelines to the Commission and the EMA.<sup>62</sup>

Nonetheless, accountability mechanisms should be applicable for how these guidelines are subsequently generated by the Commission and the EMA, to ensure that the basic procedural norms of European administrative law are respected. In general, further research

<sup>56</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 64.

<sup>57</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 65.

<sup>58</sup> European Court of Auditors, Management of Conflict of Interest in selected EU Agencies, Special Report 15/2012. See also: Vos (2016), p. 218.

<sup>59</sup> Busuioac (2013), pp. 75-113.

<sup>60</sup> Regulation (EC) No 726/2004, OJ L 136, 30 April 2004, pp. 1-33, Art. 64(1).

<sup>61</sup> Chapter 1, Section 5.3.

<sup>62</sup> Chapter 3, Section 4.

is certainly required about the accountability of the European administration when it acts globally and implements global standards into the EU regulatory framework. Introducing specific accountability mechanisms could be proposed, for the participation of the EU administration in the setting of global regulatory standards, and their ensuing implementation into the EU regulatory framework, given that, as was shown in Chapter 1,<sup>63</sup> global standards influence many regulatory areas.

### 3. LEGAL ACCOUNTABILITY – JUDICIAL REVIEW OF ICH GUIDELINES WITHIN THE EU

Examining the potential of judicial review through the Court of Justice to address the legitimacy deficits of the ICH guidelines is certainly counterintuitive, as the Court does not have jurisdiction over global bodies like the ICH. What this section will assess, however, is whether the Court could critically assess the use of the implemented standards in the European Union, including questions regarding their (global) origin. It was set out in Chapter 2 that in the *Kadi* case,<sup>64</sup> the Court looked beyond the EU measure in assessing a Regulation based on a UN Security Council Regulation, and assessed the underlying UN procedure and its compliance with fundamental rights protection in the Union. A similar logic could be applied with regard to the ICH guidelines and their implementing measures in the EU. The Court would then examine the implementation of ICH standards through the EMA, and question whether these standards live up to the procedural requirements that have to be fulfilled for such administrative guidance measures in the EU.

Raised at many points in this research before, the distinction between hard law and soft law is also central to the assessment of the access to judicial review of administrative guidelines. As the ICH guidelines are implemented in the form of EMA guidelines on the European level, the question of judicial reviewability is mainly connected to the reviewability of EMA guidelines. As was proven in Chapter 5, the ICH guidelines can influence Commission guidelines or legislation, however, a judicial review of the respective Commission guidelines would only allow for challenging the specific (part of) the ICH guideline that has influenced the Commission guideline, and not the whole implemented ICH guideline as such. The focus of this section will therefore be the review of EMA guidelines as the implementation mechanism through which the ICH guidelines become an integral part of EU pharmaceutical regulation. Nonetheless, in general the judicial review of Commission guidelines and EMA guidelines is subject to comparable requirements under European procedural law, as will also become clear in the following analysis.

#### 3.1 *Judicial review of the legality of EMA guidelines implementing ICH guidelines*

The competences of the Court with regard to the legality review are laid down in Article 263 TFEU. Within the review system established in this Article, the range of measures reviewable under this Article is limited to the power to annul ‘legislative acts’ as well as ‘acts of the European Parliament and the European Council intended to produce legal effects vis-à-vis third parties’.<sup>65</sup> Moreover the review power of the Court also encompasses ‘acts of bodies, offices or agencies of the Union intended to produce legal effects vis-à-vis third parties’.<sup>66</sup> Central entry points for access to judicial review are thus the authorship of the act

<sup>63</sup> Chapter 1, Section 2.1.

<sup>64</sup> Joined cases C-402 and 415/05P, *Kadi & Al Barakaat International Foundation v. Council & Commission*, ECLI:EU:C:2008:461. See: Chapter 2, Section 5.1.

<sup>65</sup> Art. 263(1) TFEU.

<sup>66</sup> Art. 263(1) TFEU.

as well as legally binding nature or the intention to produce legal effects vis-à-vis third parties.

The question of whether these EMA guidelines can be assessed by the Court is central to the judicial accountability of ICH implementation in the European risk regulation framework. With regard to the authorship of the measures in question, the guidelines as adopted by the CHMP are attributed to the European Medicines Agency. As Article 263 TFEU since the Lisbon Treaty also encompasses ‘agencies’ amongst the bodies and institutions subject to judicial review, the authorship criterion is, in principle, fulfilled.<sup>67</sup> As the EMA implements the ICH guidelines literally,<sup>68</sup> the authorship of the adopted guideline lies *de facto* with the ICH, while *de iure* – through the CHMP adoption – it is transformed into an act of the Agency.

The key to whether the CHMP guidelines will be amenable to judicial review is thus the question of whether they are legally binding or produce legal effects. Guidelines are ‘atypical instruments’<sup>69</sup> in the sense that they are not mentioned within the range of legally binding instruments available to the EU institutions as laid down in Article 288 TFEU. Still, it is important to assess whether these guidelines are capable of producing legal effects towards third parties. As for guidance documents, the question of judicial reviewability in the light of these considerations is not sufficiently clarified for Commission nor agency guidelines.<sup>70</sup> The soft law nature of a measure, in the jurisprudence of the Court, does not generally exclude legal effects. In the words of the *Grimaldi* judgment, often cited in the context of soft law in the EU, the Court acknowledged that a recommendation, although non-binding, ‘cannot therefore be regarded as having no legal effect’.<sup>71</sup> In *Grimaldi* this legal effect concerned the duty of Member States to take the recommendation in question into account.<sup>72</sup>

Whether or not a measure has legal effects is determined by its substance and not necessarily through its form.<sup>73</sup> One important factor is the procedural stage at which a measure is adopted, since where the act in question marks the end point of a procedure as opposed to a preparatory document, it is more likely that the act will be amenable to judicial review due to its final character.<sup>74</sup> This is exemplified by an action brought against a scientific opinion of the EMA, which constitutes a preparatory step towards the marketing authorisation granted by a Commission Decision. In the *Olivieri* case the action was dismissed and the opinion declared not to be subject to judicial review due to its preparatory

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<sup>67</sup> D. Chalmers, *European Union Public Law: Text and Materials*, 2<sup>nd</sup> Edition, (Cambridge: Cambridge University Press, 2010), p. 399. The inclusion of agencies in Art. 263 TFEU is a codification of previous case law of the Court (Case 294/83 *Les Verts v. Parliament*, ECLI:EU:C:1986:166; Case T-411/06 *Sogelma v. EAR*, ECLI:EU:T:2008:419).

<sup>68</sup> Chapter 5, Section 2.

<sup>69</sup> A. Alemanno, ‘A Meeting of Minds on Impact Assessment – When Ex Ante Evaluation Meets Ex Post Judicial Control’, 17(3) *European Public Law* (2011), pp. 485-505, p. 493.

<sup>70</sup> Scott (2011), p. 339.

<sup>71</sup> Case C-322/88 *Grimaldi*, ECLI:EU:C:1989:646, para. 18.

<sup>72</sup> Case C-322/88 *Grimaldi*, ECLI:EU:C:1989:646, para. 16.

<sup>73</sup> Case 22/70 *Commission v. Council (ERTA)*, ECLI:EU:C:1971:32, para. 42; Case 60/81 *IBM v. Commission*, ECLI:EU:C:1981:264, para. 9.

<sup>74</sup> Chalmers (2010), p. 401. An example is the *Air France* case, where the Court admitted an oral statement by the Commission to judicial review, since the oral declaration from the Commission – that it had no jurisdiction on a merger – had the legal effect on the parties that national law was applicable to their merger. T-3/93 *Air France v. Commission*, ECLI:EU:T:1994:36.

nature.<sup>75</sup> Here, it should be acknowledged that in the case of EMA guidelines the logic of *Olivieri* does not apply, since the guidelines are not a preparatory step in a procedure leading to a binding outcome. With adoption of the guidelines the administrative procedure has ended.<sup>76</sup> Thus, these guidelines cannot be qualified as preparatory documents, which would preclude judicial review.

According to research by Ştefan, in the area of competition law the Court has acknowledged the binding legal effects of soft law measures in over 600 instances.<sup>77</sup> Still, these acknowledged legal effects are usually only in the form of a self-binding effect on the body drafting the guidance document and not a binding effect vis-à-vis third parties, with the Court relying on general principles of law like legitimate expectations as well as legal certainty and transparency.<sup>78</sup> Overall, however, the record of judicial review of guidance documents is mixed. The Court has for example declined legal effects of a Commission guideline that was declared to be an ‘internal guideline’, due to its administrative-coordinative nature, which accordingly fell short of granting rights or imposing obligations on third parties.<sup>79</sup> However, Scott points out that the Court has acknowledged legal effects of guidance documents,<sup>80</sup> where they (i) introduce an obligation that is not found in the relevant legislation,<sup>81</sup> (ii) are of decisional character in the sense that they lay down how legal obligations will be applied where the institution has discretion,<sup>82</sup> or (iii) are binding upon the Member States due to legislation.<sup>83</sup> Still, overall Scott points out that these cases are exceptional and guidance documents commonly will not be eligible to judicial review.<sup>84</sup>

One therefore has to assess whether the clarification of the legislative requirements of quality, safety and efficacy laid down in the guidelines might be qualified as introducing new obligations. Scott convincingly argued that ‘(w)hen the underlying legal obligation takes the form of an only vaguely defined framework norm, it will frequently be impossible to make a clear determination of where the boundaries of existing obligation begin and end’.<sup>85</sup>

Indeed, without performing an assessment of the content of all EMA guidelines implementing ICH standards, it seems that the EMA guidelines provide the technical specifications of what quality, safety and efficacy of medicinal products entail, and which methods can be used to prove them, rather than creating additional obligations. Generally, the technical nature of these documents seems to impair the Court from assuming review responsibilities.<sup>86</sup> Moreover, where the Court has resorted to the reasoning of a judicial review due to newly imposed obligations, a crucial factor is the imperative wording of the measures.<sup>87</sup> As discussed before, the EMA guidelines come with a disclaimer that underlines

<sup>75</sup> Case T-326/99 *Nancy Fern Olivieri v. Commission*, ECLI:EU:T:2003:351, para. 53.

<sup>76</sup> See also: Ehnert (2015), p. 141.

<sup>77</sup> Ştefan (2013). These include judgements as well as orders and opinions.

<sup>78</sup> Ştefan (2012), p. 893; Ştefan (2014), pp. 359-379.

<sup>79</sup> Case C-443/97 *Spain v. Commission*, ECLI:EU:C:2000:190, para. 28.

<sup>80</sup> Scott (2011), p. 341.

<sup>81</sup> Example provided by Scott: Case C-366/88 *France v. Commission (Internal instructions)*, ECLI:EU:C:1990:348.

<sup>82</sup> Example provided by Scott: Case T-374/04 *Germany v. Commission*, ECLI:EU:T:2007:332.

<sup>83</sup> Example provided by Scott: Case C-311/94 *IJssel-Vliet Combinatie BV v. Minister van Economische Zaken*, ECLI:EU:C:1996:383.

<sup>84</sup> Scott (2011), p. 329.

<sup>85</sup> Scott (2011), p. 342.

<sup>86</sup> E. Korkea-aho, ‘Better Judicial Review? EU Courts and the Smart Regulation Agenda in Implementing Chemicals Regulation’, 6(3) *Legisprudence* (2012), pp. 397-423, p. 413.

<sup>87</sup> Scott (2011), p. 340. See: Case C-325/91 *France v. Commission*, ECLI:EU:C:1993:245, para. 14; Case C-366/88 *France v. Commission (Internal instructions)*, ECLI:EU:C:1990:348.

their voluntary nature and the possibility to deviate, while the language used in the guidelines cannot be qualified as imperative.<sup>88</sup> A statement published by the EMA indicates that this intention to produce legal effects is lacking:

‘Within the framework of the pharmaceutical legislation, scientific guidelines do not have legal force and the definitive legal requirements are those outlined in the relevant Community legislative framework (Directives, Regulations, Decisions etc.) as well as appropriate national rules.’<sup>89</sup>

Although the Court is willing to look beyond such legal disclaimers, together with the fact that the language of the guidelines is not imperative, overall, legal effects of EMA guidelines in the light of the current jurisprudence will in all likelihood be excluded.

However, the legal effect of a guidance document might also be based on its decisional nature in indicating how the institution will apply its discretion, even where the intention to produce legal effect is lacking. The Court has ruled that guidelines can have legal effects: by publishing the guidelines the institution limits its own discretion to deviate when it takes the decisions directed at individuals that are governed by these guidelines.<sup>90</sup> As was pointed out in Chapter 3, the EMA guidelines do have legal effect on the agency itself.<sup>91</sup> Nevertheless, Article 263 TFEU is very specific in requiring legal effect vis-à-vis third parties in order to subject acts of agencies to judicial review. Thus, in order to translate into the option for judicial review, the legal effects of the guidelines with regard to the drafting body are not sufficient to trigger review under Article 263 TFEU.

The core principle with regard to judicial review is that ‘an action for annulment is available in the case of all measures adopted by the institutions, whatever their nature or form, which are intended to have legal effects’.<sup>92</sup> To enquire about this, first of all, the intention of the drafting body is relevant. It is decisive whether the act brings about a change in the legal position of a third party, which requires the imperative nature of the language used to be assessed.<sup>93</sup> As pointed out before, the guidelines are published with a disclaimer and although the website states that the EMA ‘strongly encourages’<sup>94</sup> the compliance with these guidelines, a legal obligation is not conveyed by the agency. Looking for example at the Good Manufacturing Practice Guideline, the language is not perceived as imperative as the document is characterised as ‘intended to provide guidance’, or ‘intended to help’; it is clarified that ‘the term “should”, which is used consistently throughout the guideline, ‘indicates recommendations’.<sup>95</sup> Therefore, an intention to produce legal effects vis-à-vis third parties cannot be deduced.

However, the question is whether intention is a necessary requirement or if in case of

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<sup>88</sup> See: Chapter 3, Section 4.

<sup>89</sup> EMA, Status of EMEA scientific guidelines and European Pharmacopoeia monographs and chapters in the regulatory framework applicable to medicinal products, EMEA/42371/2008, 11 September 2008 – corr.

<sup>90</sup> Case T-374/04 *Germany v. Commission*, ECLI:EU:T:2007:332, para. 114.

<sup>91</sup> See Chapter 3, Section 4.2.4.

<sup>92</sup> Case C-57/95 *France v. Commission*, ECLI:EU:C:1997:164, para. 7.

<sup>93</sup> Chalmers (2010), p. 400.

<sup>94</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/-general\\_content\\_000043.jsp&mid=WC0b01ac05800240cb](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/-general_content_000043.jsp&mid=WC0b01ac05800240cb), (emphasis added), last accessed: 3 April 2017.

<sup>95</sup> EMA, Note for Guidance on Good Manufacturing Practice for Active Pharmaceutical Ingredients, November 2000, CPMP/ICH/4106/00, p. 5.

lack of intention it will be looked at whether measure in fact produces legal effects.<sup>96</sup> Thus, whether the *de facto* effect on the marketing authorisation applicants that the guidelines have would be sufficient. In Chapter 3 it was shown that the guidelines are reinforced through legislation and are presented as marking the route to obtaining a marketing authorisation by communicating what, in the view of the agency, are acceptable methods to prove the quality, safety and efficacy of a medicinal product.<sup>97</sup> Although it is possible to deviate from the guidelines, this needs to be duly justified, entailing a shift in the burden of proof.<sup>98</sup> Nonetheless, at least currently the Court does not seem to be open to such arguments. The Court ruled in the case of *Chemische Fabrik Kreuzler*, with regard to a Commission guidance document on medical devices that a ‘guidance document (...), which is not one of the legal acts of the European Union referred to in Article 288 TFEU, cannot be of a legally binding nature or enforceable against individuals’.<sup>99</sup> The Court thus simply brushed aside the question of capability of producing *de facto* legal effects without closer assessment.

Still, in a preliminary ruling procedure under Article 267 TFEU, a case with regard to a German standard might suggest that the refraining approach of the Court from technical standards might have been overcome at least to some degree. In its preliminary ruling in the *Fra.bo* case the Court took an interesting stance about technical standards set by private standard-setters in Germany.<sup>100</sup> The German DVGW sets standards for technical appliances like copper fittings and certifies products in compliance with these standards. Products carrying this certificate are presumed to comply with the conditions of the Regulation on General Conditions for Water Supply (AVBWasserV).

The preliminary ruling asked whether this is in conformity with the free movement of goods. The AVBWasserV allows for proving compliance with its conditions through a different procedure, other than obtaining certification. Despite this, the Court was convinced that the other procedure was not used in practice, due to procedural ambiguities and additional costs. The Court thus ruled that ‘the DVGW, by virtue of its authority to certify the products, in reality holds the power to regulate the entry into the German market of products’,<sup>101</sup> and that the free movement conditions also apply in this case although the DVGW is a private body. Although the situation in this case differs from the question on whether the standards in EMA guidelines can have legal effects through the key element of certification by a private body, and the free movement of goods context in the *Fra.bo* case, it is still to be argued that through *Fra.bo* the Court expressed its consciousness of the quasi-legal effects of standardisation on trade. This ruling is highly relevant for the European standards adopted in the context of the ‘New Approach’ in the European Union standardisation regime.<sup>102</sup>

Whether the Court would be inclined to adopt a parallel approach also in the judicial review under Article 263 TFEU and for risk regulation standards is unclear, and will require clarification in front of the Court. However, as was shown with regard to the guidelines adopted by the CHMP, the industry is more inclined to follow the guidelines than to justify

<sup>96</sup> European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433, p. 56ff.

<sup>97</sup> Chapter 3, Section 4.

<sup>98</sup> Chapter 3, Section 4.

<sup>99</sup> Case C-308/11 *Chemische Fabrik Kreuzler & Co. GmbH v. Sunstar Deutschland GmbH*, ECLI:EU:C:2012:548, para. 23.

<sup>100</sup> Case C-171/11 *Fra.bo SpA v. Deutsche Vereinigung des Gas- und Wasserfaches eV (DGVW)- Technisch Wissenschaftlicher Verein*, ECLI:EU:C:2012:45.

<sup>101</sup> Case C-171/11 *Fra.bo SpA v. Deutsche Vereinigung des Gas- und Wasserfaches eV (DGVW)- Technisch Wissenschaftlicher Verein*, ECLI:EU:C:2012:45, para. 31.

<sup>102</sup> Schepel (2013), pp. 521-533. Also: Van Gerstel & Micklitz (2013), pp. 145-182.

deviation.<sup>103</sup> Thus, in principle an analogy could be drawn here. What could stand in the way of applying a similar reasoning is the fact that it is not the EMA that grants the marketing authorisation, but the Commission. Thus unlike in the DVGW in the *Fra.bo* case, the EMA sets the guidelines and applies them, but is not the final decision maker on marketing authorisation. Although the Commission arguably only ‘rubber-stamps’ the EMA scientific opinion,<sup>104</sup> the Court in *Schering Plough* clearly denied the review of EMA acts due to their ‘merely’ advisory nature.<sup>105</sup>

Thus, evaluating the probability of judicial review of CHMP guidelines implementing ICH standards today, it has to be concluded that the situation is unclear, but in all likelihood the Court would currently deny judicial review responsibilities due to the lack of legal effects of these guidelines. Overall, there exists a ‘mismatch between the actual effects of soft law and the readiness of the CJEU to acknowledge them’.<sup>106</sup>

Even if an EMA guideline would be qualified as a reviewable act, the procedure under Article 263 TFEU has limited standing as only privileged applicants being the Members States, the European Parliament, the Council, or the Commission have the unlimited capacity to challenge an act. None of these privileged applicants have shown an interest in challenging an EMA guideline implementing an ICH guideline.

Judicial review could be an interesting option for pharmaceutical companies or non-governmental organisations that do not agree with the guideline. However, for non-privileged applicants, access to judicial review is delimited through the strict standing requirements of the Court established in the *Plaumann* case, which require an applicant which is not one of the privileged applicants, but another natural or legal person, to prove that the measure in question is of direct and individual concern before access to judicial review is granted.<sup>107</sup> This means that natural or legal persons, like for example a pharmaceutical company or a stakeholder group, can only in very limited circumstances challenge a legislative measure and the mandate to participate in the ICH contained therein. Although heavily criticised, the *Plaumann* criteria has largely prevented legal challenges brought by non-privileged applicants until today.<sup>108</sup>

The introduction of judicial review of ‘regulatory acts’ under Article 263(4) TFEU, which only requires direct effect and no further implementing measures, also does not benefit the position of a private party wanting to challenge an EMA guideline. First of all, it is not entirely clear if guidelines would indeed qualify as a regulatory act. The court defined regulatory acts as ‘acts of general application apart from legislative acts’.<sup>109</sup> Although the

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<sup>103</sup> Chapter 3, Section 4.2.2.

<sup>104</sup> R. Dehousse, ‘Delegation of Powers in the European Union: The Need for Multi-principals Model’, 31(4) *West European Politics* (2008), pp. 789-805, p. 799.

<sup>105</sup> Case T-133/03 *Schering-Plough Ltd. v. Commission and EMEA*, ECLI:EU:T:2007:365, para. 23.

<sup>106</sup> Ştefan (2014), p. 367.

<sup>107</sup> Case C-25/62 *Plaumann & Co. V. Commission of the European Economic Community*, ECLI:EU:C:1963:17. The established criteria were reconfirmed in Case C-50/00P, *Unión de Pequeños Agricultores (UPA) v. Council of the European Union*, ECLI:EU:C:2002:462. See: Hofmann, Rowe & Türk (2011), p. 812ff.

<sup>108</sup> Criticism of the requirements of direct and individual concern is and *inter alia* voiced by: A. Arnulf, ‘Private Applicants and the Action for Annulment since *Codorniu*’, 38(7) *Common Market Law Review* (2001), pp. 7-52; P. Craig, ‘Legality, Standing and Substantive Review in Community Law’, 14(4) *Oxford Journal of Legal Studies* (1994), pp. 507-537; C. Harlow, ‘Towards a Theory of Access for the European Court of Justice’, 12(1) *Yearbook of European Law* (1992), pp. 213-248.

<sup>109</sup> Case T-18/10 *Inuit Tapiriit Kanatami and Others v. Parliament and Council*, ECLI:EU:T:2011:419; Case T-262/10 *Microban International Ltd and Microban (Europe) Ltd v. European Commission*,

guidelines are acts of general nature not adopted in accordance with a legislative procedure under Article 289 TFEU, many ambiguities with regard to the concept of regulatory acts persist. More importantly, however, the adoption of an EMA guideline as such does not directly affect the legal situation of a private party; this only happens through its application in the marketing authorisation procedure. Even if a marketing authorisation is rejected due to non-compliance with a guideline, it is the actual decision of the Commission refusing to grant a marketing authorisation that will be the act that changes the legal position and, thus, forms the act that should be challenged.

### 3.2 *Judicial review through other means: challenging binding decisions*

An alternative option to challenging EMA guidelines directly, are cases where EMA guidelines are part of the challenge of a binding decision of the Commission. This logic of assessment of an act through the assessment of another act, is exemplified in the *Artegodan* case, where the withdrawal of marketing authorisations through several Commission decisions was challenged.<sup>110</sup> In this case the Court acknowledged that the review of the Commission decision did require looking beyond the decision to its scientific base, which was a CPMP opinion.<sup>111</sup> It then continued to assess whether the CPMP in its opinion provided sufficient reason for its decision and the transparency of the process, which ‘ensures that the substance in question has undergone a detailed and objective scientific assessment’.<sup>112</sup> As pointed out in Chapter 5, in this case the Court also looked into the substance of a CPMP note for guidance relevant for the case.<sup>113</sup> Thus, while the CPMP opinion itself was not amenable to judicial review, it has been assessed on its procedural qualities since it provided the scientific basis for a contested binding measure.

A similar situation could also occur in case of the ICH guidelines, as the following discussion of the *Acino* case will show.<sup>114</sup> The dispute between the company Acino AG and the European Commission surrounded the recall of the drug Clopidogrel due to irregularities in an Indian manufacturing site, which amounted to a breach of the good manufacturing practice prescribed in the European Union. The inspection report showed that 70 protocols (manufacturing standards) had been manipulated and, furthermore, other Good Manufacturing Practice requirements such as those relating to the used equipment, the premises in which the manufacturing was conducted, and the cleaning of both equipment and premises were not followed in the factory. Due to the danger of contamination or cross-contamination, the factory was removed from the list of sites authorised to manufacture Clopidogrel. The marketing authorisation of the medicine was suspended and concerned products manufactured in the factory had to be recalled. Thus, due to its non-compliance

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ECLI:EU:T:2011:623; Case C-583/11 *Inuit Tapiriit Kanatami and Others v. Parliament and Council*, ECLI:EU:C:2013:625.

<sup>110</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, para. 39.

<sup>111</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, paras. 198 and 199.

<sup>112</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, para. 200.

<sup>113</sup> Chapter 5, Section 4.3.

<sup>114</sup> Case T-539/10 *Acino AG v. Commission*, ECLI:EU:T:2013:110. The case has been appealed: Case C-269/13P *Acino AG v. Commission*, ECLI:EU:C:2014:255.

with Good Manufacturing Practice, the marketing authorisations had to be changed as the factory was removed from the sites that were allowed to manufacture the drug.

The Good Manufacturing Practice applicable in European pharmaceutical law is enshrined in a variety of legislative and non-legislative measures,<sup>115</sup> whereas some of the requirements have their origin in ICH guidelines.<sup>116</sup> Whether non-compliance with ICH GMP requirements (in their implemented form) were also among the breaches that led to the closure of the Indian factory is not clear from the case, and is difficult to reenact as the Court does not go into detail on which GMP norms exactly have been breached. However, the technical requirements regarding the Good Manufacturing Practice, including cleaning of the equipment and premises, are subject to ICH guidelines.<sup>117</sup>

In the *Acino* case the applicant did not contest the validity of the Good Manufacturing Practice as such, but rather the consequences the Commission – relying on the CHMP – drew from the non-compliance, namely the change of the marketing authorisation and the order recall of the products. It is, however, conceivable that an applicant could contest the validity of the applied norms. One reason could be the origin in ICH guidelines, which would force the Court to look into the process of establishing ICH guidelines. In the *Artegodan* case the Court clarified that the scope of its review would cover whether ‘the consultation of the CPMP is *inter partes* and transparent, it ensures that the substance in question has undergone a detailed and objective scientific assessment, based on a comparison of the most representative scientific opinions (...)’.<sup>118</sup> In this regard, for example the involvement of potentially conflicted industry experts in the ICH standard-setting process, this would certainly leave room to argue that the standards do not represent the outcome of an objective scientific assessment. Also, the legitimacy gaps related to stakeholder participation and transparency could be raised before the Court under this logic.

However, even if the Court would indeed be ready to extend the *Artegodan* logic to EMA guidelines and thereby look at their formal legality – which then would need to include taking into account the ICH decision-making procedure in case the EMA guidelines are essentially ICH guidelines – the review would be incidental and limited only to the cases of a decision that finds its explicit base in an implemented ICH guideline. Moreover, it is highly questionable whether the Court would indeed reach out and closely examine the decision-making procedure at the ICH level. In the *Kadi* case, the Court felt entitled to look into the UN origin of the contested measure and assess alleged procedural flaws. However, in *Kadi* the claims concerned the infringement of fundamental rights of individual persons, whereas in the case of ICH guidelines, the flaws are more of an administrative nature and do not directly infringe individual rights.

Therefore, the judicial review of binding measures does not provide a satisfactory solution in order to address the procedural deficits of ICH guidelines that are implemented in the EU. The analysis has thus shown that under the current judicial review mechanisms the Court currently will not provide for judicial review of the ICH-based norms, apart from the very incidental cases where binding decisions will be based on EMA implemented ICH guidelines. Even in these cases the probability of an in-depth consideration of the ICH process is low. Although the Court in *Fra.bo* seems open to acknowledging the *de facto* effects of standards, it does not seem ready to generally open up to such a logic, and as a

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<sup>115</sup> Chapter 3, Section 4.1.3.

<sup>116</sup> Chapter 5, Section 4.2.

<sup>117</sup> Chapter 5, Section 4.2.

<sup>118</sup> Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283, para. 200.

consequence admit the judicial review of scientific and technical standards.

As long as a judicial grappling with the legitimacy flaws in measures such as the implemented ICH norms is lacking and the Court turns a blind eye on these instruments, substantial parts of the risk regulation framework will escape the enforcement of the Union's commitment to participatory openness, transparency and the independent scientific expertise it bases its decisions on. This also means that the Court loses the possibility of actively shaping the procedural legitimacy of soft law.<sup>119</sup> Moreover, this limited judicial review fails to acknowledge the actual effects of guidelines on the institutions, the Member States, individuals and even the Courts itself, as assessed in the previous chapter. Given these effects, the guidance measures should be subject to judicial review. Thus, in keeping the distinction between hard and soft law with regard to Court access, the reality of increasingly unclear borders between hard and soft law is ignored in practice.<sup>120</sup> In their seminal article of 2007 Scott and Sturm find a different role for European courts in general and the Court in specificity, depicting it as 'catalyst'.<sup>121</sup> In the context of the 'new governance' debate,<sup>122</sup> they pronounce the ability of the Court to promote norms of participation, reason-giving, expertise as well as transparency and accountability.<sup>123</sup> This judicial review is then meant to enhance the legitimacy of governance mechanisms through 'shared values justifying the elaboration and implementation of public norms'.<sup>124</sup> In this regard, calls for judicial review of various types of soft law mechanisms have been voiced frequently in the literature.<sup>125</sup>

#### 4. GLOBAL PHARMACEUTICAL STANDARDS AS CHALLENGE FOR EUROPEAN LAW – THE POTENTIAL FOR JURIDIFICATION

This research has shown that the legitimacy flaws that derive from the implementation of global pharmaceutical standards which do not live up to essential EU administrative law principles gives rise to several challenges for European law, which are also not counterbalanced by domestic accountability mechanisms.

First of all, the case of global pharmaceutical standards has shown that transferring regulatory power to the global level comes with the danger of circumventing EU administrative principles and procedures that would apply to norms of the same legal status if they would originate in the EU administrative bodies. This is highly problematic since the norms, although often taking the form of soft law, have considerable legal and practical effects on administrative bodies in the EU and the Member States, regulated industries and European citizens in general, that is, as consumers of medicinal products.

Moreover, the participation of the European actors – in this case the Commission and the European Medicines Agency – in global standard-setting bodies is not sufficiently regulated in the Treaties and subject to diverse degrees of regulation in the respective sectoral secondary legislation. Overall, this means that the limits to global activities of the EU administration, and the procedural rules applicable to these activities, are non-transparent and incoherent. Taking into account the sheer multitude of global regulatory cooperation initiatives, this means that they essentially become unfathomable. The need for a

<sup>119</sup> Ştefan (2014), p. 366; Scott (2011), p. 349ff.

<sup>120</sup> Ştefan (2014), p. 368.

<sup>121</sup> J. Scott & S. Sturm, 'Courts as Catalysts: Rethinking The Judicial Role in New Governance', 13(3) *The Columbia Journal of European Law* (2007), pp. 565-594.

<sup>122</sup> For more detail on new governance in the European Union see Chapter 1, Section 4.3.

<sup>123</sup> Scott & Sturm (2007), p. 565.

<sup>124</sup> Scott & Sturm (2007), p. 567.

<sup>125</sup> See amongst others: Scott (2011), pp. 329-355; Senden (2013), pp. 57-75; Ştefan (2014), pp. 359-379.

more coherent approach certainly holds true not only with regard to the pharmaceutical standards dealt with in this research: Chapter 1 has shown that global standards are also implemented in European regulation in a large variety of other areas.<sup>126</sup>

As currently, implementation of these global standards and the participation of the EU administration in global standard-setting initiatives are insufficiently regulated on the EU level, there is certainly a need for a comprehensive framework for interaction between global standards and EU risk regulation. Therefore the juridification of the participation of European administration in global standard-setting bodies, and procedural rules on the acceptability of global standards received in the EU, could address the legitimacy flaws caused by the current situation. Juridification should be understood as a ‘process through which an activity becomes subjected to legal regulation or more detailed legal regulation’.<sup>127</sup>

This is exemplified in the field of ‘European standards’ developed under the New Approach.<sup>128</sup> Since the inception of the New Approach in 1985 the Commission has for example worked towards increasing stakeholder participation possibilities for consumer representatives, and the transparency of the standard-setting process in the private bodies, which develop the European standards.<sup>129</sup> The procedure of setting European standards has been juridified through the adoption of Regulation 1025/2012 on European standardisation.<sup>130</sup> Basic procedural requirements on transparency and stakeholder participation are now laid down in the regulation, such as Article 5 stating standardisation organisations need to ‘encourage and facilitate an appropriate representation and effective participation of all relevant stakeholders’ and specify procedural stages such as ‘the technical discussion on proposals’ in which stakeholder participation is to be encouraged.<sup>131</sup>

The following short analysis will, therefore, explore two routes for the juridification of the interplay of global standards and EU risk regulation, in the area of pharmaceuticals and beyond, providing indications for future research rather than establishing a full legal framework. It will be examined whether the introduction of ex-ante and/or ex-post procedures in the process of implementing global standards would mitigate the legitimacy flaws carried over from the global to the European level. Furthermore, the possibility of juridification of the interface between global standards and EU risk regulation through an EU administrative procedure act will be discussed.

#### 4.1 *Introducing ex-ante and ex-post procedures in the process of implementation*

The flaws that have been identified with stakeholder participation, independent expertise and transparency are imported into the European regulatory framework through the implementation of the ICH guidelines through the European Medicines Agency. As pointed out in Chapter 1, global standards are not binding upon the EU and therefore, unlike

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<sup>126</sup> Chapter 1.

<sup>127</sup> L. Blichner & A. Molander, ‘Mapping Juridification’, 14(1) *European Law Journal* (2008), pp. 36-54, p.42. See also: J. Habermas, *The Theory of Communicative Action – Volume 2* (Boston: Beacon Press, 1987), p. 359.

<sup>128</sup> Schepel (2013), pp. 521-533. For further detail on European standards see: See Chapter 1, Section 2.2.

<sup>129</sup> Vos (1999), p. 289ff.; Schepel (2005), p. 242ff.

<sup>130</sup> Regulation (EU) No 1025/2012 of the European Parliament and of the Council of 25 October 2012 on European standardization, OJ L 316, pp. 12-33.

<sup>131</sup> Regulation (EU) No 1025/2012 of the European Parliament and of the Council of 25 October 2012 on European standardization, OJ L 316, pp. 12-33, Art. 5.

international agreements, are not automatically integrated into the legal order of the EU, but require a connecting measure that integrates them into the EU legal framework.<sup>132</sup>

One way to counterbalance legitimacy gaps in the adoption process of a standard on a global level, would be the introduction of an implementation procedure on the European level allowing for the safeguarding of European procedural standards. One could for example imagine applying the full procedure applicable to the drafting of EMA guidelines to ICH guidelines, instead of only endorsing them through the agency.<sup>133</sup> This would then include a renewed discussion of the scientific content of the norms in the respective scientific bodies of the agency and an additional public consultation procedure.

However, introducing an implementation procedure is only a theoretical possibility, as it is obstructed by the fact that once the standard is adopted on the global level it cannot be changed in the implementation, as otherwise the standard would not lead to the envisaged global harmonisation. Therefore, any *ex post* procedures on the European level, like applying the European style public consultation procedure, would be window-dressing as the guideline as adopted on the ICH level cannot be changed. The Rules of Procedure of the ICH Assembly provide that 'to achieve true international harmonisation, it is important that the ICH Guidelines are implemented consistently by all ICH Regulators'.<sup>134</sup>

Rather than applying an *ex post* procedure, one could also imagine safeguarding procedural standards *ex ante*, through preparatory procedures in the EU before the standard is set on the global level. One procedural mechanism that could be applied on a European level, to provide stakeholders with more participatory means to influence the work of the ICH, would be to systematically have preliminary discussions of ICH standards with stakeholders in open meetings, while the drafting process in the ICH is still underway. This happens in the US, where the FDA holds public meetings before every ICH meeting to seek stakeholder input.<sup>135</sup> The existing means of stakeholder participation in the EMA, for example the stakeholder working parties,<sup>136</sup> could be used as channels to disseminate information on ICH standards and to identify interested stakeholders that could participate in public ICH preparation meetings.

However, although this might improve the participatory means of stakeholders other than industry, it would probably only provide a mechanism for European based stakeholder groups and – similarly to the consultation procedure already in place – also does not grant stakeholders direct access to the discussions in the ICH. Given that the guidelines will be subject to discussion on the ICH level afterwards, there is also no guarantee that the input provided by stakeholders on the EU level will persist throughout the discussions in the ICH. Finally, such an *ex ante* approach would only address the gaps in participation of other stakeholders, while issues such as the independence of experts involved in the ICH and the transparency of the ICH process cannot be addressed through EU measures. Thus, *ex ante* mechanisms in the EU will only mitigate the flaws in the ICH process to a certain degree.

Therefore, introducing *ex ante* or *ex post* procedures with regard to the implementation of global standards does not efficiently address the challenges posed by the interface of global standards and EU pharmaceutical regulation.

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<sup>132</sup> Chapter 1, Section 3.3.

<sup>133</sup> Chapter 3, Section 4.1.2.

<sup>134</sup> ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, p. 4.

<sup>135</sup> Berman (2011b), p. 16. Information on the public meetings and summaries can be obtained via: [www.regulations.gov](http://www.regulations.gov), last accessed: 3 April 2017.

<sup>136</sup> Chapter 6, Section 2.2.

#### 4.2 *EU Administrative Procedure Act with a global dimension*

What has become clear in the general analysis of the role of European actors in global standard-setting carried out in Chapter 1, is that there is no clear mandate for the Commission to participate in global standard-setting initiatives. It has been shown that only in case of standard-setting in international organisations and binding legal agreements, does the Treaty provide answers to whether the EU is competent to act externally and who should act on behalf of the EU.<sup>137</sup> Where the remit of traditional international law is left, as is the case with many standard-setting initiatives that are not established as international organisations or through binding international agreements, the boundaries of the Commission's mandate to participate in such bodies are less clear. Moreover, whereas the mandate for the European Medicines Agency as well as other agencies can be located in their founding regulation, it is rather superficial, without providing for procedural rules or limitations with regard to the bodies the agencies participate in or their role in implementing global standards. The complex regulatory structures with diverse types of global standard-setting bodies, as well as the specific position of the EU – which in many areas shares the competence for external action with the Member States – certainly complicate the development of clear legal mandates.

What has become clear, moreover, is that the existing rules with regard to the EU's interplay with global standards, just like EU administrative law in general, are very fragmented. Administrative bodies like the Commission and agencies are bound to the specific procedural rules established in the respective regulatory field such as pharmaceuticals regulation.<sup>138</sup> Of course the rules applicable to EU administrative actors in principle also guide their activities on the global level,<sup>139</sup> therefore, the core principles of participation, transparency and independent expertise apply to internal as well as external activities. However, one needs to look into the rules and practices of the European administrative actors in order to uncover how the treaty principles are applied in specific policy areas. Additionally, these sector-specific rules are drafted for the internal regulatory and administrative tasks, while often ignoring the global activities of these bodies. In the face of globalisation, the fragmented nature of EU administrative law causes problems. The existing internal divergence in procedural standards runs the risk of further sectoralisation. The administrative authorities of one regulatory branch (namely pharmaceuticals) cooperate with their counterparts globally, establishing not only vertically split administrations,<sup>140</sup> but with administrative bodies establishing their own sector-specific global cooperation practices.

A unified European law regulating administrative procedures could address this fragmentation. As pointed out in Chapter 2, the EU does not currently dispose over an Administrative Procedure Act, although the European Parliament<sup>141</sup> and the European

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<sup>137</sup> Chapter 1, Section 5.1.

<sup>138</sup> Chapter 2, Section 5.2; See also: Hofmann, Schneider & Ziller (2014), p. 46f.; Hofmann (2009), p. 50; Research Network on European Administrative Law (ReNEUAL), 'Introduction to the ReNEUAL Model Rules/ Book I – General Provisions', 2014, p. 8.

<sup>139</sup> Mendes (2014), p. 396.

<sup>140</sup> Möllers (2005a), p. 379.

<sup>141</sup> European Parliament, European administrative procedure law, Resolution of 15 January 2013, 2012/2024 INL, P7\_TA(2013)0004; European Parliament, A regulation for an open, efficient and independent European Union administration, Resolution of 9 June 2016, 2016/2610 RSP, P8\_TA(2016)0279.

Ombudsman have undertaken initiatives.<sup>142</sup> However, where the EU would adopt such an act, it could introduce provisions on the participation of European administrative bodies in global administrative bodies. It could establish rules regarding the implementation of global standards through administrative measures, which would safeguard the procedural standards applicable in the EU, where the decision-making power is outsourced to the global level.

Comparable to the juridification of European standards, where basic rules for transparency and participation in the standard setting process were laid down in a regulation, a European administrative procedure act could set basic rules for global standards received in the EU. The EU could perform a legitimacy test, before integrating norms that are developed externally into its regulatory framework.<sup>143</sup> Deriving such basic procedural rules would require a comparative study of the interface of global standards with various areas of European regulation. Therefore, this research is not the right place to indicate such common rules. However, the analysis in Chapter 6 has already uncovered certain principles and norms against which global standards can be assessed in the area of pharmaceuticals.<sup>144</sup> The rules and practices identified in this research regarding balanced participation, public consultations, conflict of interest and transparency could form a starting point for developing general minimum standards, which could be incorporated into an EU act of administrative procedure.

Where the European administrative procedure act should provide a meaningful tool to address the implementation of global standards, it also has to cover the development of administrative soft law, given that – as in the case of the ICH – the adoption of such guidance documents might be the route to implementing global standards. The ReNEUAL project is careful on the matter of administrative rule-making, stating that: ‘As much as the drafters would hope for the ReNEUAL Model Rules to be applied as far as possible, as a matter of good administrative practice, to informal acts of general application, at this stage of the procedure, the drafters of the book decided not to suggest any binding obligation to do so.’<sup>145</sup> However, the proposal attached to the European Parliament Resolution in 2016 includes ‘administrative activities of the Union’s institutions, bodies, offices and agencies’, while only excluding legislative as well as judicial procedures, and ‘the adoption of non-legislative acts directly based on the Treaties, delegated acts or implementing acts’.<sup>146</sup> Therefore, the proposal as drafted by the Parliament would cover the drafting of EMA guidelines.

The Commission has not used its right of legislative initiative with regard to a European Administrative Procedure Act and it is not certain if it might cover the adoption of administrative guidance. However, this research has shown that soft law standards form an important part of the regulatory framework. Neglecting them in a law governing European administrative procedures means that a large part of administrative activity will not be covered, although it has (indirect) legal effects on the regulated individuals in practice. Moreover, as argued above, the adoption of an EU Administrative Procedure Act would provide the EU with a chance to remedy the challenges posed by global standards, and their implementation in the EU.

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<sup>142</sup> European Ombudsman, *The European Code of Good Administrative Behaviour*, available via: <http://www.ombudsman.europa.eu/en/resources/code.faces#/page/1>, last accessed: 3 April 2017.

<sup>143</sup> Chapter 2, Section 5.1. See also: Devaux (2013), p. 862.

<sup>144</sup> Chapter 6.

<sup>145</sup> Research Network on European Administrative Law (ReNEUAL), ‘ReNEUAL Model Rules on EU Administrative Procedure Book II – Administrative Rulemaking’, 2014, p. 46.

<sup>146</sup> European Parliament, *A regulation for an open, efficient and independent European Union administration*, Resolution of 9 June 2016, 2016/2610 RSP, P8\_TA(2016)0279, Art. 2.

## 5. CONCLUSION

While the previous chapter was concerned with applying EU administrative law to global pharmaceutical standards set by the ICH, suggesting norms and practices that could be uploaded to the global level, this chapter was focused on examining remedies within the EU against the legitimacy flaws that are integrated in European pharmaceutical regulation, through the implementation of global pharmaceutical standards.

It became clear that the political accountability of EU administrative actors participating in global standard-setting and implementing global standards in the EU does not currently provide an effective remedy. Although it was shown that the Council and the European Parliament especially would dispose of efficient accountability mechanisms, these are not used to introduce meaningful accountability for the implementation of global pharmaceutical standards. Other bodies also fail to fill this gap, as the Pharmaceutical Committee would have the required expertise, but not the sanctioning power. The Ombudsman and the Court of Auditors have not made use of their – arguably more limited – powers to hold the Commission or the European Medicines Agency accountable with regard to their ICH activities. This research has raised the question of whether specific political accountability mechanisms for the global regulatory activities of the EU administration might be beneficial.

Moreover, it was shown that currently the legal accountability through judicial review of implemented ICH guidelines is lacking, as due to their non-binding nature the EMA guidelines are not subject to systematic legality review. Incidentally, they may become subject to judicial review where they form the scientific basis of a challengeable act. However, this only provides for an incomplete accountability framework – if any at all. With this, the Court misses an important opportunity to acknowledge the *de facto* legal effect of administrative guidance and the global standards which it can implement.

Finally, the juridification of the interface between global standards and EU pharmaceutical regulation was discussed. It became clear that neither *ex-ante* nor *ex-post* procedures in the process of implementing global standards can fully remedy the legitimacy deficits identified in Chapter 6. Therefore, it was proposed to subject the participation of EU administrative actors in global standard-setting bodies and the implementation of global standards in the EU to general juridification in an EU administrative procedure law. In this regard, while the norms identified in Chapter 6 can form a starting point, future research is required to identify common standards addressing global standards from the perspective of various sectors of European regulation.



## Chapter 8: Conclusion

### 1. THE RISE OF GLOBAL STANDARDS AND QUESTIONS REGARDING THEIR LEGITIMACY – AN APPRAISAL

Risk regulation standards are important regulatory tools to address the risks faced by society today. They are defined as voluntary expertise-based rules, constituting measurable criteria by which a product or a production process or service can be evaluated on the basis of technical or physical conditions. Thus they are not limited to regulating the compatibility of technical components, but regulate the safety and quality of products and production processes. Standards form an important mechanism for regulating markets and protecting consumers and the environment.

Given the increasingly interconnected markets and the complexity of risks faced by society today, such risk regulation standards cannot effectively prevent risks from materialising where they are established by national constituencies in isolation. Therefore, risk regulation standards-setting increasingly takes place on the global level. Global standards are often set through the cooperation of domestic regulators. This means that besides the traditional actors of international law-making, such as diplomats or members of government, the administration gains importance as a global actor. Within standard-setting there is also increasing reliance on another actor at the global level: private parties. In this regard, public interest non-governmental organisations (NGO) or private economic actors such as businesses and private organisations either take part in standard-setting or set standards on their own. The rise of private actors in standard-setting is often attributed to their expertise and knowledge of state-of-the-art technology.

These actors perform their standard-setting tasks in four different types of bodies: (i) international organisations, (ii) transnational regulators networks, (iii) private standard-setting bodies, and (iv) public-private partnerships. Within these bodies regulators and/or private actors work together in various degrees of cooperation and formalisation. With a high degree of legal formalisation due to their treaty basis, international organisations traditionally work on topics concerning 'high politics' topics. Now, they are increasingly taking over regulatory tasks too. Some international organisations have also opened up to input from private actors through networks of experts they consult, or through granting them observer status. In the case of transnational regulators networks, the members are domestic regulators, taking part in the network in their administrative capacity rather than as representatives of the state. Little legal formalisation takes place as the network is formed through regular interactions in contrast to the establishment of a legal entity. Also, private bodies are increasingly engaging in the setting of regulatory standards. Finally, the research proposed the term public-private partnership, for bodies with various degrees of formalisation reaching from legally established entities to loose networks. The common characteristic of public-private partnerships is the cooperation between government or administrative actors and profit or non-profit private organisations, leading to joint decision-making. Overall, the institutional landscape of global standard-setting thus mirrors the complexity of the risks that it aims to address, creating a kaleidoscope of interaction frameworks and formalisation.

Where such standards are developed on the global level, they are mainly addressed to regulators for implementation into the domestic frameworks. However, through this implementation they then also affect private actors as second level addressees. Thus, although global standards do not constitute legally binding measures, they can be soft law in the sense that they can give rise to (indirect) legal effects. Indeed, irrespective of their voluntary nature global standards have proven to be very effective regulatory measures and can become *de facto* binding based on their origin in regulatory cooperation, their epistemic

legitimacy and sometimes also due to reinforcement through law.

For regulators as well as regulated industries the reliance on global standards has several benefits. First of all, since these standards create a level playing field for global trade, they relieve producers from the duty of either having to adapt their products or (where applicable) their marketing authorisation application to every single constituency in which they want to sell their products. Moreover, in the case of standard-setting through regulatory cooperation, the regulators benefit from the sharing of resources with their foreign counterparts. In the case of standard-setting with the participation of private parties, they benefit from the expertise that the private parties have in these very technical and scientific regulatory fields. Especially the latter point, the access to expertise, is often emphasised at times when public trust in the capability of the regulators to address the risks society is facing day-to-day is decreasing.

Therefore, global standards set through the cooperation of regulators with varying degrees of involvement of private actors, often in the form of soft law, do not easily fit into the traditional conceptualisation of international law, and very much exemplify the shift from 'government' to 'governance'. With this shift, however, questions of legitimacy arise as the classical forms of legitimation in democratic nation states are left behind. These questions become more pressing, as it was established that global standards become *de facto* binding upon regulators, affect private individuals and, furthermore, may contain political choices within the decisions depicted as technical and scientific.

Global standard-setting with its basis in regulatory cooperation and the participation of private parties is often justified through the rhetoric of efficiency and effectiveness benefits. Therefore, a potential route to assess the legitimacy of global standard-setting is the input and output legitimacy theory by Scharpf, which in essence proposes counterbalancing a lacking democratic basis through the capacity of the authority to solve a collective problem. Indeed, due to a lack of global collective identity and flawed participatory mechanisms caused by a dominance of industrial representation, the input legitimacy of global standard-setting is defective. However, the legitimisation of these standards based on their capability of effectively solving collective problems does not provide a viable option in the case of global risk regulation standards either. This is caused by the inherent nature of risk regulation, where – especially in the face of uncertain risks – regulatory problems do not necessarily have a 'correct' answer. The question of whether a standard efficiently addresses a risk will be evaluated differently depending on a certain regulatory approach, risk adversity and diverging social or ethical values. As an administration cannot establish the 'correct' answer to a regulatory problem it requires the input of diverse interests in the regulatory process, which means that in case of risk regulation standards the argumentation of counteracting defects in the input legitimacy with output legitimacy becomes a circular argument, as output legitimacy requires input legitimacy. Thus, the argument of legitimacy through efficiency and effectiveness is not constructive in the case of global risk regulation standards.

This research has, therefore, adhered to assessing the legitimacy of global standards through the lens of legal-rational legitimacy, and specifically the adherence to procedural standards established by administrative law. The adherence to administrative law standards has the potential to make the exercise of administrative power on the global level more accountable, democratic, and protective of rights of individuals. In this regard, two questions arise: first of all, can administrative law be applicable to hybrid public-private or even private form of governance? Second of all, even more fundamentally, does a form of administrative law applicable to global standard-setting bodies even exist?

For the first question, it has been argued in this research that as hybrid and private global standard-setting bodies in essence carry out traditionally public tasks, the procedural

standards that are applicable in similar situations to public bodies should also apply in these cases. This will require a focus on the functions that a body carries out as opposed to its legal nature. Drawing from the theory of 'International Public Authority' this research advocates applying administrative law norms to global standard-setting bodies where their activities are implemented into national and regional regulatory frameworks, as is the case with regard to global risk regulation standards.

Concerning the second question, it has been shown that currently no established administrative law framework is applicable to global standard-setting bodies. However, the scholarships of global administrative law and international administrative law respectively are advancing to fill this void. The GAL scholarship works towards the identification of overarching principles of global administrative law, in the form of participation, transparency, reason-giving and legality. This scholarship stresses the broadening of the application of global administrative law to institutions that do not conform to traditional international law establishment forms, making it an attractive theoretical framework for the assessment of global standard-setting bodies. Nonetheless, where it identifies overarching principles it does not fill them with substantial rules on how for example transparency is ensured. Therefore, although it is very valuable in the identification of current practices, global administrative law does not provide the necessary detail to allow a legitimacy assessment of global standard-setting bodies. The international administrative law scholarship takes a different approach in the sense that it conducts analysis of certain reference areas, in which it analyses the legal consequences of global administrative activity from the perspective of national, supranational and international law. The arising international administrative law, identified through this reference area analysis, is then synthesised to identify an overall legal framework of international administrative law. Here, however, a substantive body of international administrative law is not currently in existence.

Thus, although an administrative law applicable to global standard-setting bodies is currently evolving it still faces problems in identifying its sources. For the research at hand, both scholarships provided important insights. The Global Administrative Law scholarship identified a practice of global administrative bodies to submit themselves to certain core principles, and argued for a broadening of the concept of global administrative law beyond traditional international law bodies to hybrid and private forms of governance. The international administrative law scholarship approach of examining this practice in the context of national, supranational and international law is promising since it aims at the development of a coherent framework applicable to global administrative action. The research at hand used this contextual approach to advocate for the analysis of global standard-setting from a European administrative law perspective.

Overall, it can be concluded that global standard-setting is an increasingly important phenomenon, the impact of which is often hidden behind the stressing of the voluntary and merely technical nature of these standards. However, upon closer examination it became clear that these standards increasingly shape our regulatory reality and affect the rights of individuals. Nonetheless, currently a large variety of global standard-setting bodies are mushrooming in the global administrative space without being subject to institutional or procedural limitation in the form of an established body of administrative law.

What, therefore, presents itself as a legitimacy problem at the global level, is however carried over into the domestic regulatory frameworks, as the standards meander their way into these systems through implementation. Accordingly, addressing these legitimacy challenges is indispensable not only for the standard-setting bodies themselves, but also for the implementing states and regional organisations.

## 2. EUROPEAN RISK REGULATION – ADDRESSING THE CHALLENGES OF GLOBALISATION

Global standards also have become an important part of European risk regulation. On the one hand, the European administrative bodies take part in global standard-setting, and, on the other hand, these global standards then find their way into the European risk regulation framework through implementation.

The implementation of global standards in the European Union, was shown to be a phenomenon that is certainly increasing in the globalisation age, although already in 1984 in the *Beer Purity* case the Court obliged Member States to take into account the global foodstuffs standards of the Codex Alimentarius Commission. Moreover, several legislative measures such as the General Food Law and the chemicals regulation REACH contain references to global standards, obliging the European administrative bodies to take such global standards where they take regulatory measures into account. Thus, the implementation and compliance with global risk regulation standards is an important trait of European risk regulation, openly promoted both through legislative and judicial means.

Moreover, the Commission – sometimes with the support of European agencies – takes part in global standard-setting initiatives. This participation needs to be based on a mandate, which has been shown to raise complex issues with regard to European institutional law and questions of external representation. This needs to be distinguished between the representation of the EU in international organisations, which engage in standard-setting, and the more loosely organised forms of standard-setting initiatives. The legal framework around the participation of the Commission in less legally formalised harmonisation initiatives is not very clear. This, therefore, requires a case-by-case analysis of every informal standard-setting body the Commission participates in. In this regard, a clarification of the rights and duties of the Commission with regard to the participation in global standard-setting bodies that are not legally formalised through a Treaty provision would increase the legal certainty with regard to the Commission as a global actor.

The participation of European agencies in global standard-setting is governed by the provisions of the founding regulations of the agencies. The agencies benefit from the cooperation with their international counterpart through knowledge and resource sharing. Furthermore, their role as global actor contributes to the consolidation of their expert status within the EU and with regard to their foreign counterparts. Whereas the agencies cannot act as official representatives of the EU or enter into binding agreements, their internal role as independent expert bodies has made them a valuable support for the Commission in global standard-setting initiatives. The increasingly important external role of the European agencies, and also the burgeoning diversity in how this role is carried out, has not gone unnoticed in the literature and the European institutions. The Common Approach on decentralised agencies adopted by the Commission, the European Parliament and the Council in 2012 called for structuring the approach to international relations of European agencies. Currently, however, the external actions of agencies only find their limitations in remarkably vague mandates in their founding regulations, which neither provide procedural requirements nor set limits to the subjects of cooperation.

Thus, overall, with regard to the participation of European administrative bodies in global standard-setting, the legal delimitation of these activities is currently very fragmented. It is dependent upon the global standard-setting body in question, the regulatory area concerned, and also the question of which EU body is participating. Given the large variety of global standard-setting bodies and the increasingly important role of the European administration as global actors within such bodies, a more structured approach to external action would highly benefit the legal certainty and transparency of such activities.

It has been shown that global standards are received in the EU through implementation, as their lack of legal binding nature requires a connecting measure to make them applicable in the EU. The implementation into the regulatory framework of the EU either takes place via binding legislation or through soft law measures. A binding legislative measure can either contain a binding static reference to a standard in force at the time of adoption, a dynamic binding reference, which includes also future developments of a certain standard, or the incorporation of an obligation to take a certain standard into account. As the global standards are implemented in the EU, queries with regard to their legitimacy also arise out of a European perspective, as it has to be questioned why standards that become applicable in the EU and affect rights of individuals are not subjected to the same procedural rules that would have to be followed where their adoption would take place in the Union originally. The Court of Justice used a similar reasoning in the *Kadi* case where it stressed the importance of the EU constitutional principles and rights these protect, and established that these cannot be undermined through international agreements and obligations following from such agreements.

Although the *Kadi* case was ruled under different circumstances, this research has advocated a similar logic for the case of global standard-setting, in assessing global standards against the benchmarks of European administrative law, and specifically the principles of participation, independent expertise and transparency, which find their basis in the EU's commitment to democracy. The outsourcing of regulatory power to the global level should not lead to derogation from the principles applicable to administrative action in the EU. In the application of European administrative law to global standards, a difficulty arises from the absence of a uniform European law on administrative procedures, which leads to a situation where for every global standard it has to be assessed how comparable norms in the EU are established in the respective policy field. Thus for example, the benchmarks for comparison to the pharmaceutical standards set by the International Council for Harmonisation are the procedures applicable to pharmaceutical standards. In the EU, these are implemented in the form of guidelines adopted by the European Medicines Agency.

It has to be concluded that, given the increasing importance of global standards, a commitment in the EU towards democracy and good governance will remain incomplete as long as it does not address questions of global standards. A transfer of regulatory power to the global level opens the door to the implementation of global standards into the regulatory framework of the EU, which falls short of respecting essential procedural requirements for administrative action in the EU.

### 3. ICH GUIDELINES AND THEIR IMPLEMENTATION IN THE EUROPEAN UNION

Global pharmaceutical standards and their implementation in the EU have proven to be a highly relevant field for the exemplary in-depth study of global risk regulation standards. The implementation of global standards set by the ICH in the regulatory framework of the EU raised several questions about the legal nature of the ICH and the norms it develops, as well as the legitimacy of the ICH standards.

#### 3.1 *The ICH as global standard-setter*

The ICH has become the leading global source for pharmaceutical standards, which it adopts in the form of guidelines. This body, originally established by the regulators and representatives of the research-based pharmaceutical industry of the US, EU and Japan, has successfully harmonised the marketing authorisation requirements with regard to the quality, safety and efficacy of pharmaceuticals in these three regions and beyond to a significant extent. Through its recent reform, it has opened up membership to other regulators and

industry associations, while the six founding members still retain considerable privileges. The institutional structure of the ICH is characterised by a two-tier separation with the Assembly and the Management Committee as main governing bodies, and the forming of scientific consensus on specific harmonisation topics in the Expert Working Groups. This structure is supported by the ICH secretariat.

Before the reform, questions about the legal nature of the ICH remained unaddressed by the body itself. The ICH was established informally, operating largely on a meeting basis and without a treaty or other legal foundation. This meant that under traditional international law, the ICH lacked legal personality. With the ICH reform, the legal qualification of the ICH has changed, being reestablished under private law in the form of an international non-profit association under Swiss law. As this research has shown, however, the ICH can still be qualified as a public-private partnership, characterised by the participation of regulatory and industry representatives of all institutional levels. In this regard, the ICH heavily depends on the expertise provided by both industry and regulators in order to form the guidelines. It, therefore, epitomises the increasing institutional diversity of interaction at the global level and, through the membership rights it grants to industry representatives, the rise of private actors in global governance.

The ICH sets its guidelines in a five-step decision-making procedure that relies on consensus as the core decision-making principle. However, both the Management Committee and the Assembly may proceed to voting where consensus cannot be reached. Through the reform, steps have been undertaken in order to better distinguish the role of industry and regulators in the ICH process. The members representing industry cannot prevent the choice of a topic for harmonisation in a voting procedure in the Assembly. They will neither be considered for the consensus nor for voting on the final adoption of a guideline in the Assembly. Also, the recommendation of the Management Committee on the adoption of a guideline will be decided on without interference of the members representing industry. While the process has therefore become more regulator driven, industry representatives still take part in the forming of the scientific consensus in the Expert Working groups, and can exert substantial influence on the content of the ICH guidelines. Thus, the relationship between industry and regulators in the ICH can still be qualified as co-regulation.

These guidelines are not legally binding on the ICH members. However, the members are politically committed to implement the standards. This commitment together with the firm basis of the guidelines in consensus as well as their recognition as state-of-the-art standards has led to the success of the ICH. Currently over 60 guidelines are adopted by the ICH and all of them are implemented in the regulatory framework of the Founding Regulatory Members, while Standing Regulatory Members and new Regulatory Members are also expected to implement the standards in the near future. Thus, although there is no legal obligation to implement the guidelines, they become *de facto* binding on the members.

Where the technical requirements are harmonised, the recognition of each other's assessment would be the next logical step for the ICH members. The adoption of the Common Technical Document (CTD), which standardises the marketing authorisation application format through the ICH regions, has certainly increased the feasibility of such an endeavour. Furthermore, decision-making on marketing authorisations in the global ICH setting might also be an option to consider. However, giving up the full decision-making power of which pharmaceuticals should be allowed onto the respective markets is a major commitment and entails significant sovereignty losses. Currently, this does not seem politically achievable and given the legitimacy concerns that have been identified by this research, it might not be preferable. With the extended membership of the ICH, mutual recognition of marketing authorisations also becomes less likely.

### 3.2 *EU pharmaceutical regulation and its global standards*

The core of European pharmaceutical regulation is formed by the marketing authorisation procedures that medicinal products have to undergo in order to be sold on the internal market. There are three main routes to obtaining marketing authorisations: a national one, a decentralised/mutual recognition route, and a central route on the European level. Thus, pharmaceutical regulation in the EU knows a divergence in degree of integration according to the type of pharmaceutical concerned and the question of where it should be marketed. Still, within all these routes, the requirements to prove the quality, safety and efficacy of the medicinal product concerned are harmonised.

An important finding of this research is the prominent role of non-binding measures in the form of agency and Commission guidelines in the governance of pharmaceuticals on the European level. While legislation will set out the overarching lines of the regulatory policies and the procedures to execute them, they require further scientific and technical details, which are then elaborated on in post-legislative guidance documents. This allows for a faster adaptation to new scientific findings and technical progress, as their amendment or replacement is less procedurally burdensome than to amend or adopt legislation. Thus, guidance documents have been used extensively in the regulation of pharmaceuticals, harmonising the regulatory requirements in the centralised, decentralised and national marketing authorisation procedures.

The guidelines governing pharmaceuticals in Europe have been identified as soft law measures. Although they are not legally binding, they have to be taken into account in drafting the marketing authorisation applications according to Annex 1 of Directive 2001/83/EC and Article 6(1) of Regulation (EC) 726/2004. The guidelines are usually adopted on an explicit basis in the legislation and have been qualified by the EMA itself as ‘quasi-binding’. They can only be deviated from by marketing authorisation applicants upon provision of a justified reason and, therefore, present which standards are acceptable to prove the quality, safety and efficacy of a medicinal product from a scientific point of view. In practice, the leeway for marketing authorisation applicants to deviate from the guidelines is rather small. The high costs involved in pharmaceutical development certainly deter companies from risking deviation from the established standards given the shifting burden of proof. Moreover, these guidelines also affect Member States as the guidelines work through into the national marketing authorisation procedures. Finally, the adoption of guidelines has a self-binding effect on the adopting body, derived from the principles of equal treatment, legitimate expectations and legal certainty.

The analysis has shown that 19% percent, thus approximately one fifth, of the European Medicines Agency guidelines originate in the ICH. Importantly, these ICH guidelines are usually applicable to all therapeutic classes of drugs, while the EMA guidelines often address specific therapeutic classes. Thus, the ICH guidelines will often provide the overarching standards, while additional EMA guidelines will supplement these ICH guidelines for more specific therapeutic classes. Once the ICH guidelines are implemented into the regulatory framework of the EU, through adoption by the Committee for Medicinal Products for Human Use (CHMP) in the EMA, they have the same legal status as guidelines originating in the EMA being ‘quasi-binding’. While the share of ICH guidelines within the EMA guidelines is not equally distributed amongst the different guideline categories (quality, biological, and so on), it was shown that there is also a significant degree of interaction between the guidelines originating in the EMA and the ICH guidelines. It was as well established that over 70% of the remaining guidelines, which originate in the EMA independently from ICH guidelines, contain references to ICH guidelines. Therefore, ICH guidelines form an important part of the scientific guidance provided by the EMA.

In addition to the implementation of the ICH guidelines through the EMA, references to ICH guidelines can also be found in Commission guidelines and, at least in one instance, the ICH guidelines have been shown to exert influence on Commission guidelines, leading to amendments. Moreover, in the case of the Good Manufacturing Practice and the Good Clinical Practice, our analysis has proven influence on European legislation, sometimes even with literal transposition of ICH standards into binding EU law. In addition, the potential use of the ICH guidelines in the Court of Justice as interpretative aid has been pointed out.

Therefore the ICH guidelines, which originate as soft law on the global level, deeply penetrate the European pharmaceuticals regulation and it becomes increasingly difficult to identify the borderline between global standards and the EU risk regulation framework.

### *3.3 Legitimacy challenges arising from the implementation of global pharmaceutical standards in the European Union*

The research has shown the significant influence of global pharmaceutical standards on the EU and has, in general, argued for the application of European administrative law to such standard-setting bodies. With respect to the implementation of ICH standards through the European Medicines Agency, this has revealed that the ICH procedure does not live up to the procedural standards applied to comparable measures in the EU, concerning participatory openness, independence of expertise, and transparency.

Where the ICH guidelines are adopted by the EMA in the CHMP, they do not undergo the usual guideline adoption procedure. In the true spirit of harmonisation, the guidelines, once they are adopted by the ICH, can only be implemented into the framework of the EU without undergoing further changes. Thus, where the procedure of the adoption of ICH guidelines does not live up to the procedural standards as set by EU administrative law, these flaws are carried over into the European regulatory framework.

It has been shown that there are differences with the participation of stakeholders in the decision-making process. In the ICH, the representatives of the research-based industry have obtained full membership status and have become co-regulators of their own products. This partnership between regulators and industry is not counterbalanced with an equal institutionalised role of other stakeholders in the ICH process, since these can only become observers. The only other possibility to provide input into the ICH standard setting-process for other stakeholders remains the public consultation procedure carried out in the adoption process of the guidelines. However, the consultation takes place after the scientific consensus has been formed and, furthermore, no feedback is provided on how the comments have been used. Therefore, in the ICH harmonisation process, the industry has become a privileged stakeholder, while this pronounced status is not counterbalanced with similar roles for other stakeholders.

In the EU, participation of civil society in the decision-making process forms an important administrative law principle. The European Medicines Agency has institutionalised the participation of patients as well as doctors' associations in its Management Committee, as well as in some of its scientific committees and through special working parties. Moreover, where stakeholders do not form part of these working parties, they can engage in the guideline drafting process in the public consultation. The EMA public consultation process has the advantage that consultation takes place twice within the procedure: first at the beginning of the drafting process for the concept paper, and secondly after the adoption of the draft guideline. This means that stakeholders are involved in the early stages of the drafting process. In addition to that, the comments received are published on the website, and a summary is drafted by the rapporteur that will also provide notes on how comments have been taken into account. Therefore, when compared to the European

procedural standards, the ICH participation mechanisms are insufficiently balanced, making the pharmaceutical industry a co-regulator while limiting the influence of other stakeholders from providing comments in the public consultation procedure. This is highly problematic where pharmaceutical regulation is aimed at achieving a balance between public health and industrial interests.

Where the independence of expertise is concerned, the ICH has not undertaken any measures to address the conflicts of interest, which are inherent in its institutional structure as regulator-industry partnership. In the EU, however, the prevention of conflicts of interest has become an important procedural standard, especially in risk regulation process. The European Medicines Agency has also adopted extensive conflict of interest rules. All persons taking part in the work of the agency have to declare direct and indirect interests in the pharmaceutical industry. In essence, direct interests in the pharmaceutical industry will prevent the participation of an expert in the work of the agency including the drafting of scientific guidelines, whereas other forms of conflicts of interest will lead to different limitations. Moreover, conflicts of interest are recorded in the minutes of the respective meetings.

The role of the industry in the ICH process fundamentally counteracts the independence of expertise and is flawed when assessed in the context of EU administrative law. While the inherent industry involvement in the ICH will not be changed, lessons can be learned from the EMA rules on making conflicts of interest transparent. Here, the ICH could require the representatives in the ICH bodies and also the experts in the working groups to publish conflict of interest declarations, that would make such conflicts visible internally and externally.

Both the observations about participation as well as independent expertise are closely linked to the overall transparency of the ICH process. While efforts have been undertaken to make the ICH process more transparent, it was shown that a lack of transparency persists about the decision-making procedure and especially the membership of the expert working groups. Assessed against the transparency commitment enshrined in European administrative law and the practice of the European Medicines Agency, several advantages of the EMA approach have been identified. The members taking part in the EMA guideline adoption process are known and their conflict of interest declarations are published. Moreover, through the public consultation procedure the decision-making process becomes more visible and the influences exerted by stakeholders can be evaluated from the summary of comments received.

Thus, although the ICH guidelines, once they are adopted by the CHMP, will have the same status as all other EMA guidelines, this research has shown that their adoption process does not conform to general principles of EU administrative law. Therefore, through outsourcing the regulatory powers of pharmaceutical standard-setting to the global level, essential principles of EU administrative law are bypassed. This is of concern not only with regard to pharmaceutical regulation at the EU level, as the standards work through to the regulatory systems of the Member States. It is essential that the EU evaluates the global standards it integrates into its regulatory framework with regard to the core criteria of EU administrative law, as otherwise these general principles are 'hollowed out'.<sup>1</sup>

These legitimacy flaws are not mitigated through political or judicial accountability in the EU. While in general political accountability frameworks for the Commission and the EMA are in place, this does not lead to meaningful accountability for their role in the ICH or the implementation of ICH standards in the EU. Specific political accountability mechanisms for the global regulatory activities of the EU administration might fill this

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<sup>1</sup> Mendes (2012), pp. 988-1022.

lacuna. When it comes to judicial review, it was pleaded for acknowledging the de facto legal effect of administrative guidance and the global standards implemented through these soft law measures. This would allow for subjecting the administrative measures which are implementing global standards to legal accountability.

#### 4. THE INTERFACE OF GLOBAL AND EUROPEAN ADMINISTRATIVE LAW – AN OUTLOOK

While this research has shown that the ICH standards raise several concerns where they are measured against the benchmark of EU administrative law, it should be considered that on the global level analogous general principles are arising too. The global administrative law scholarship has identified a tendency in global administrative practice of bodies subjecting themselves to administrative law principles like transparency and participation, regardless of their public, private or hybrid nature. European administrative law has developed with a strong focus on general principles, which are defined and further developed especially through jurisprudence, and are often based on the practices in the Member States. This has, therefore, been argued to serve as a valuable source of inspiration for the evolving global administrative law.

This research has shown that the ICH, like other global administrative bodies, has indeed in the recent past undergone procedural changes in order to better define the different roles of regulators and industry in the decision-making procedure. Moreover, it has taken several measures to increase the transparency of its process. Thus, the tendency towards the development of certain best practices on the global level that has been observed by the GAL scholarship can also be confirmed for the ICH. However, in the interviews conducted for this research it was indicated that these procedural changes to a certain degree originated in concerns about how the ICH process would be evaluated in a domestic context.<sup>2</sup> For the European actors in the ICH process, the debates in the EU on transparency and independence in the area of pharmaceutical regulation also led to a re-thinking of whether the ICH harmonisation process can be justified. Thus, as is also advocated by the international administrative law scholarship, global administrative activity needs to be assessed in context. Taking inspiration from EU administrative law can provide valuable insights for the evolving administrative law on the global level. Moreover, given the interaction between the European and the global level, in terms of European actors participating in the global standard-setting and the standards finding their way back into the EU, the question of compatibility of global standard-setting with European administrative law procedural standards cannot be avoided.

What can be learned from the analysis of the implementation of ICH standards into the pharmaceutical regulation of the EU is that global administrative law could be further defined through ‘uploading’ certain EU administrative law norms and practices, in order to ensure a more balanced participation of stakeholders, more transparency with regard to conflicts of interest, and also the decision-making procedures. Moreover, beyond the specific case of pharmaceuticals, the administrative law applicable in other regulatory areas in the EU could also provide insights that can valuably contribute to the formation of an administrative law applicable to global standard-setting bodies. Further research on this is certainly required. This also holds true from a European perspective, as the implementation of global standards is a phenomenon that spans over a multitude of regulatory areas in the EU’s risk

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<sup>2</sup> Interview with an official of the EFPIA, conducted in Brussels on 17 February 2015, notes on file with the author; Interview with two officials of the European Commission, conducted in Brussels on 17 February 2015, notes on file with the author.

regulation framework.

Finally, the implementation of global standards in EU risk regulation also raises challenges for EU administrative law. Developing an administrative law framework for the external activities of European administrative bodies will be an important task of the legal scholarship and also the European institutions in the face of an ever-globalising regulatory reality. It was proposed to use the opportunity provided by the discussions surrounding an EU law of administrative procedure, to subject the participation of EU administrative actors in global standard-setting bodies, and the implementation of global standards in the EU to general juridification.



## Valorisation Addendum

### *The social relevance of this research*

This research examines the influence of global risk regulation standards on EU pharmaceutical regulation and it questions the legitimacy of the implementation of these standards in the EU risk regulation framework. The societal relevance of the legitimacy of risk regulation standards, especially where they aim to promote and protect public health is evident. For instance, several incidents of regulatory failures in the history of the EU – the most vivid memory is certainly left by the BSE crisis – have shown that risk regulation processes should be subjected to critical legal examination especially with regard to procedural aspects with the aim to improve the quality of the measures taken as well as the public trust in such risk regulation measures.

The value of critically examining global standards does not only hold true in the health related area of pharmaceutical regulation, but the societal relevance of examining the legitimacy of global standards is broader. A 2016 study by the Bertelsmann Stiftung “Globalisierungsangst oder Wertekonflikt?” (Fear of globalization or conflict of values?) identified a direct link between fears of the general public related to globalization and the recent electoral successes of populist parties. This demonstrates that it is essential to obtain an in-depth understanding of the legal and regulatory consequences of globalization, to identify and address the situations in which such fears may be valid and to de-mystify incorrect claims. This research wants to contribute to this debate, by providing a better understanding of the effects of global standard-setting – a regulatory response to globalization – on risk regulation in the Union and by making suggestions on how to improve global standard-setting processes.

More in detail, this research contributes to analysing the impact of global pharmaceutical standards on the regulation of medicinal products in the EU. A discussion of global standards in the regulation of pharmaceuticals in this regard is especially important, as also in the area of pharmaceuticals public trust in regulatory capacity has been shaken by the ‘Mediator Scandal’ as well as the withdrawal of the anti-diabetes drug Avandia as addressed in the Introduction of this research. The research at hand shows that the global standard-setting processes of the International Council for Harmonisation (ICH) – when compared to EU procedural norms of transparency, participation and independence of expertise – is indeed flawed. These procedural defects negatively affect the legitimacy of their implementation in the Unions regulatory framework for pharmaceuticals. The research also identified a political and judicial accountability gap for the implementation of these standards in the EU. However, the study also suggests that ‘uploading’ of procedural benchmarks from the EU to the global level can improve the ICH standard-setting process.

In addition, the identification of such procedural norms can also contribute to the forming of a body of administrative law on the global level. This research aims to contribute to the societal debate on a shift from government to governance, including the shift of decision-making from the national to the global level. Regulating global standard-setting processes can contribute to addressing the legal challenges posed by abandoning traditional forms of legitimation and accountability in the national states.

From a EU perspective this research is important, as it identified an incoherent approach to the participation of EU bodies in global standard-setting initiatives. It also showed that the subsequent implementation of such standards in the EU is subject to fragmented, policy-specific processes. The EU functions as a ‘gatekeeper’ for these standards as they are regulating the internal market, where they affect not only EU but also national regulators, the companies producing the regulated products and also the consumer that buys

the regulated product. Therefore, it is necessary that the Union develops a better understanding of the impact of global standards and coherently regulates them.

*The beneficiaries of this research*

In addition to the academic audience, this research is mainly addressed to the regulators and policy-makers responsible for pharmaceuticals but also to regulatory authorities involved in global standard-setting in other regulatory areas. It is primarily concerned with regulatory bodies in the EU, but is also relevant to non-EU participators in global standard-setting. Moreover, it is of relevance for global standard-setting bodies, such as the ICH. It aims to improve the regulatory process of standard-setting in terms of its participatory openness, transparency and independence of expertise, though concrete recommendations. However, the findings may also contribute to the more general public debate on how to carry out regulatory standard-setting processes on the global level.

Also, public interest representatives will benefit from the findings and recommendations of this research as it identifies the main hurdles to participation and transparency as well as offering suggestions to overcome such hurdles. It ultimately leads to suggestions of how to improve global standard-setting in the area of risk regulation, which is beneficial for society as a whole.

Furthermore, this research challenges the presumption of risk regulation standards as merely technical and scientific voluntary measures by showing their *de facto* capability to affect the legal situation of regulators (in the EU and in the Member States) as well as the regulated companies and consumers. Besides their implementation in the form of non-binding measures, global pharmaceutical standards influence legally binding measures and are used as interpretative tools in courts. This research thereby addresses the regulators, legislators and courts, in calling for a more critical handling of these regulatory measures. The research also suggests to the EU legislator to introduce a more coherent framework for the EU's participation in global standard-setting processes and the implementation of these standard. The current framework is fragmented along different policy areas and does not contain clear accountability structures.

*Translating the results into activities and products*

Next to the thesis itself, which I plan to publish in the form of a monograph, the research has and will continue to form the subject of academic publications in chapters of edited volumes and journal articles. These publications are contributing to the debate in the EU law scholarship as well as in the academic debates addressing administrative bodies on the global level, such as the global administrative law and international administrative law scholarship. Moreover, in order to enhance the visibility of the questions raised by this research in civil society, I have already and will continue to address aspects of this research in blog posts. In addition to this I have already taken the opportunity during the interviews conducted for this research and during stakeholder dialogues in the framework of the Academic Research Network on Agencification of EU Executive Governance (TARN), to discuss the findings of this research with stakeholders such as representatives of EU regulatory bodies involved in global standard-setting.

*Innovation*

Although this research builds on the existing literature in the field of Global Administrative Law, European administrative law and European institutional law, it adds an in-depth understanding of the influence of global risk regulation standards on the European

regulation of pharmaceuticals that was lacking previously. This research also identifies in-depth the effects of these standards on different actors, such as the EU bodies implementing them as well as the Member States, and the regulated companies. Moreover, this deeper understanding of the role of these standards in the risk regulation of pharmaceuticals in the EU permitted the identification of various gaps with regard to the political and judicial accountability for the implementation of such standards in the EU.

Moreover, the detailed examination of the practices with regard to transparency, participation and independence of expertise that have been identified in this thesis contribute to the existing scholarship analysing global administrative bodies. The detailed comparison of such practices on the global level with the procedural rules applicable in the EU allowed to derive useful practices from the EU level which can be transferred to the global level. This can contribute to enhancing the legitimacy of the standard-setting process.

### *Implementation*

The findings in academic journals and a monograph published on the basis of this research will be presented not only to the academic community but also to stakeholders in the regulatory process. Through blog posts I will also provide concise information about the core arguments of this research concerning procedural standards in the standard-setting process in a way that is accessible to the general public. Moreover, copies of this thesis will be sent to the European regulatory bodies involved in the ICH, the European Commission and the European Medicines Agency, which already during the interviews conducted for this research emphasised their interest in the final thesis and the policy recommendations it contains.

With regard to the European Commission and the European Medicines Agency, which take part in the ICH process, they can use the findings in Chapter 6 regarding procedural benchmarks for participation, transparency and independence of expertise to ignite an improvement of the ICH standard-setting process. Moreover, as it became clear in Chapter 1 and 2, that the rules with regard to the EU participation in global standard-setting and the implementation of these standards are diverging between the different policy areas, lacking coherence, the research proposed also address the global administrative activities of EU bodies in a European administrative procedures act. As the adoption of a European administrative procedures act has been called for by the academic scholarship as well as the Ombudsman and European Parliament, this provides an opportunity to also advocate more coherence in the approach of the EU to global standards.



**Annex 1: List of ICH guidelines as implemented  
in the EU  
(Status: 19 March 2015)**

|                | <b>ICH Guideline</b>  | <b>Implemented in EU via</b>   |
|----------------|---|--|
| <b>Quality</b> | Q1A(R2) stability testing of new drug substances and products   | Note for guidance on stability testing: stability testing of new drug substances and products (CPMP/ICH/2736/99)   |
|                | Q1B Photostability testing of new active substances and medicinal products  | Note for guidance on the photostability testing of new active substances and medicinal products (CPMP/ICH/279/95)  |
|                | Q1C stability testing: requirements of new dosage forms   | Note for guidance on stability testing: requirements for new dosage forms (CPMP/ICH/280/95)  |
|                | Q1D bracketing and matrixing designs for stability testing of drug substances and drug products                               | Note for guidance on bracketing and matrixing designs for stability testing of drug substances and drug products (CPMP/ICH/4104/00)  |
|                | Q1E evaluation of stability data  | Note for guidance on evaluation of stability data (CPMP/ICH/420/02)  |
|                | Q1F stability data package for registration in climatic zones III and IV (this guideline is withdrawn)                        | (See: explanatory note on the withdrawal of ICH Q1F from the ICH website CPMP/ICH/421/02)  |
|                | Q2(R1) validation of analytical procedures: text and methodology  | Note for guidance on validation of analytical procedures: text and methodology (CPMP/ICH/381/95)   |
|                | Q3A(R2) impurities in new drug substances   | Note for guidance on impurities testing: impurities in new drug substances (CPMP/ICH/2737/99)  |
|                | Q3B(R2) impurities in new drug products   | Note for guidance on impurities in new drug products (CPMP/ICH/2738/99)  |
|                | Q3C(R5) impurities: guideline on residual solvents  | ICH Guideline Q3C(R5) on impurities: guideline for residual solvents (EMA/CHMP/ICH/82206/2006)   |
|                | Q3D Guideline for elemental impurities  | ICH Guideline Q3D on elemental impurities (EMA/CHMP/ICH/353369/2013)   |
|                | Q4B Evaluation of pharmacopoeial texts for use in the ICH regions<br><i>This regulation has separately adopted 16 annexes</i> | Note for guidance on regulatory acceptance of analytical procedures and/or acceptance criteria (RAAPAC) (EMA/CHMP/ICH/222007/2006)<br><i>All of the annexes have been adapted by the EMA as well</i> |

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|  | Q5A(R1) viral safety evaluation of biotechnology products derived from cell lines of human or animal origin                    | Note for guidance on quality of biotechnological products: viral safety evaluation of biotechnology products derived from cell lines of human and animal origin (COMP/ICH/295/95)           |
|  | Q5B analysis of the expression construct in cell lines used for production of R-DNA derived protein products                   | Note for guidance on quality of biotechnological products: analysis of the expression construct in cell lines used for production of R-DNA derived protein products (CPMP/ICH/139/95)       |
|  | Q5C stability testing of biotechnological/biological products  | Note for guidance on quality of biotechnological products: stability testing of biotechnological/biological products (CPMP/ICH/138/95)  |
|  | Q5D derivation and characterisation of cell substrates used for production of biotechnological/biological products             | Note for guidance on quality of biotechnological products: derivation and characterisation of cell substrates used for production of biotechnological/biological products (CPMP/ICH/294/95) |
|  | Q5E comparability of biotechnological/biological products subject to changes in their manufacturing process                    | Note for guidance on biotechnological/biological products subject to changes in their manufacturing process (CPMP/ICH/5721/03)  |
|  | Q6A specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances | Note for guidance specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances (CPMP/ICH/367/96)                              |
|  | Q6B test procedures and acceptance criteria for biotechnological/biological products   | Note for guidance on specifications: test procedures and acceptance criteria for biotechnological/biological products (CPMP/ICH/365/96)   |
|  | Q7 good manufacturing practice for active pharmaceutical ingredients   | Note for guidance on good manufacturing practice for active pharmaceutical ingredients (CPMP/ICH/4106/00)   |
|  | Q8(R2) pharmaceutical development  | Note for guidance on pharmaceutical development (EMA/CHMP/167068/2004)  |
|  | Q9 quality risk management   | ICH Guideline Q9 on quality risk management (EMA/CHMP/ICH/24235/2006)   |
|  | Q10 pharmaceutical quality system  | ICH Guideline Q10 on pharmaceutical quality system (EMA/CHMP/ICH/214732/2007)   |

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|               | Q11 development and manufacture of drug substances (chemical entities and biotechnological/biological entities) | ICH Guideline Q11 development and manufacture of drug substances (chemical entities and biotechnological/biological entities) (EMA/CHMP/ICH/425213/2011) |
| <b>SAFETY</b> |   |  |
|               | S1A need for carcinogenicity studies of pharmaceuticals   | Note for guidance on the need for carcinogenicity studies of pharmaceuticals (CPMP/ICH/140/95)   |
|               | S1B testing for carcinogenicity of pharmaceuticals  | Note for guidance on carcinogenicity: testing for carcinogenicity of pharmaceuticals (CPMP/ICH/299/95)   |
|               | S1C(R2) dose selection for carcinogenicity studies of pharmaceuticals   | Note for guidance on dose selection for carcinogenicity studies of pharmaceuticals (EMEA-CHMP/ICH/383/1995)  |
|               | S2(R1) guidance on genotoxicity testing and data interpretation for pharmaceuticals intended for human use      | ICH Guideline S2(R1) guidance on genotoxicity testing and data interpretation for pharmaceuticals intended for human use (EMA/CHMP/ICH/126642/2008)      |
|               | S3A note for guidance on toxicokinetics: the assessment of systemic exposure in toxicity                        | Note for guidance on toxicokinetics: a guidance for assessing systemic exposure in toxicology studies (CPMP/ICH/384/95)                                  |
|               | S3B pharmacokinetics: repeated dose tissue distribution studies   | Note for guidance on pharmacokinetics: repeated dose tissue distribution studies (CPMP/ICH/385-95)   |
|               | S4 duration of chronic toxicity testing in animals (rodent and non-rodent toxicity testing)                     | Note for guidance on duration of chronic toxicity testing in animals (rodent and non-rodent toxicity testing) (CPMP/ICH/300/95)                          |
|               | S5(R2) detection of toxicity to reproduction for medicinal products & toxicity to male fertility                | Note for guidance on the detection of toxicity to reproduction for medicinal products & toxicity to male fertility (CPMP/ICH/386/95)                     |
|               | S6(R1) preclinical safety evaluation of biotechnology-derived pharmaceuticals                                   | ICH Guideline S6(R1) preclinical safety evaluation of biotechnology-derived pharmaceuticals (EMA/CHMP/ICH/731268/1998)                                   |
|               | S7A safety pharmacology studies for human pharmaceuticals   | Note for guidance on safety pharmacology studies for human pharmaceuticals (CPMP/ICH/539/00)   |

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|                 | S7B the nonclinical evaluation of the potential for delayed ventricular repolarization (QT interval prolongation) by human pharmaceuticals   | Note for guidance on the nonclinical evaluation of the potential for delayed ventricular repolarization (QT interval prolongation) by human pharmaceuticals (CPMP/ICH/423/02)       |
|                 | S8 immunotoxicity studies for human pharmaceuticals  | Note for guidance on immunotoxicity studies for human pharmaceuticals (CHMP/167235/2004)  |
|                 | S9 nonclinical evaluation for anticancer pharmaceuticals   | ICH Guideline S9 nonclinical evaluation for anticancer pharmaceuticals (EMA/CHMP/ICH/646107/2008)   |
|                 | S10 photosafety evaluation of pharmaceuticals  | ICH Guideline S10 photosafety evaluation of pharmaceuticals (EMA/CHMP/ICH/752211/2012)  |
| <b>EFFICACY</b> |  |   |
|                 | E1 the extent of population exposure to assess clinical safety for drugs intended for long-term treatment of non-life threatening conditions | Note for guidance on population exposure: the extent of population exposure to assess clinical safety (CPMP/ICH/375/95)   |
|                 | E2A clinical safety data management: definitions and standards for expedited reporting   | Note for guidance on clinical safety data management: definitions and standards for expedited reporting (CPMP/ICH/377/95)   |
|                 | E2B(R3) clinical safety data management: data elements for transmission of individual case safety reports                                    | ICH Guideline E2B(R3) on electronic transmission of individual case safety reports (ICSRs) - data elements and message specification – implementation guide (EMA/CHMP/ICH/287/1995) |
|                 | E2C(R2) periodic benefit-risk evaluation report  | ICH Guideline E2C(R2) on periodic benefit-risk evaluation (PBER) (EMA/CHMAP/ICH/544553/1998)  |
|                 | E2D post-approval safety data management: definitions and standards for expedited reporting  | Note for guidance on definitions and standards for expedited reporting (CPMP/ICH/3945/03)   |
|                 | E2E pharmacovigilance planning   | Note for guidance on planning pharmacovigilance activities (CPMP/ICH/5716/03)   |
|                 | E2F development safety update report   | ICH Guideline E2F on development safety update report (EMA/CHMP/ICH/309348/2008)  |

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|  | E3 structure and content of clinical study reports  | Note for guidance on structure and content of clinical study reports (CPMP/ICH/137/95)   |
|  | E4 dose-response information to support registration  | Note for guidance on dose-response information to support drug registration (CPMP/ICH/378/95)  |
|  | E5(R1) ethnic factors in the acceptability of foreign clinical data   | Note for guidance on ethnic factors in the acceptability of foreign clinical data (CPMP/ICH/289/15)  |
|  | E6(R1) guideline for good clinical practice   | Note for guidance on good clinical practice (CPMP/ICH/135/95)  |
|  | E7 studies in support of special populations: geriatrics  | Note for guidance on studies in support of special populations: geriatrics (CPMP/ICH/379/95)   |
|  | E8 general considerations for clinical trials   | Note for guidance on general considerations for clinical trials (CPMP/ICH/291/95)  |
|  | E9 statistical principles for clinical trials   | Note for guidance on statistical principles for clinical trials (CPMP/ICH/363/96)  |
|  | E10 choice of control group and related issues in clinical trials   | Note for guidance on choice of control group in clinical trials (CPMP/ICH/364/96)  |
|  | E11 clinical investigation of medicinal products in the paediatric population   | Note for guidance on clinical investigation of medicinal products in the paediatric population (CPMP/ICH/2711/99)  |
|  | E12 principles document for clinical evaluation of new antihypertensive drugs   | ICH principles document for clinical evaluation of new antihypertensive drugs (CPMP/ICH/541/00)  |
|  | E14 the clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs            | Note for guidance on the clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic drugs (CHMP/ICH/2/04)                    |
|  | E15 definitions for genomic biomarkers, pharmacogenomics, pharmacogenetics, genomic data and sample coding categories           | Note for guidance on definitions for genomic biomarkers, pharmacogenomics, pharmacogenetics, genomic data and sample coding categories (EMA/CHMP/ICH/437986/2006)        |
|  | E16 biomarkers related to drug or biotechnology product development: context, structure and format of qualification submissions | ICH Guideline E16 biomarkers related to drug or biotechnology product development: context, structure and format of qualification submissions (EMA/CHMP/ICH/380636/2009) |

| <b>MULTIDISCIPLINARY</b> |   |   |
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|                          | M3(R2) guidance on nonclinical safety studies for the conduct of human clinical trials and marketing authorisation for pharmaceuticals  | ICH Guideline M3(R2) on nonclinical safety studies for the conduct of human clinical trials and marketing authorisation for pharmaceuticals (EMA/CPMP/ICH/286/1995)                             |
|                          | M4(R3) organisation of the common technical document for the registration of pharmaceuticals for human use  | Common technical document for the registration of pharmaceuticals for human use: organisation of the common technical document (CPMP/ICH/2887/99)   |
|                          | M4Q(R1) quality. The common technical document for the registration of pharmaceuticals for human use: quality – M4Q(R1) quality overall summary of module 2 module 3: quality                                 | Common technical document for the registration of pharmaceuticals for human use, quality overall summary of module 2 and module 3: quality (CPMP/ICH/2887/99-Quality)                           |
|                          | M4S(R2) safety. The common technical document for the registration of pharmaceuticals for human use: safety – M4S(R2) nonclinical overview and nonclinical summaries of module 2 organisation of module 4     | Common technical document for the registration of pharmaceuticals for human use, nonclinical overview and nonclinical summaries of module 2, organisation of module 4 (CPMP/ICH/2887/99-Safety) |
|                          | M4E(R1) efficacy. The common technical document for the registration of pharmaceuticals for human use: efficacy – M4E(R1) clinical overview and clinical summary of module 2 module 5: clinical study reports | Common technical document for the registration of pharmaceuticals for human use, clinical overview and clinical summary of module 2 module 5: study reports (CPMP/ICH/2887/99-Efficacy)         |
|                          | M7 assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk  | ICH Guideline M7 assessment and control of DNA reactive (mutagenic) impurities in pharmaceuticals to limit potential carcinogenic risk (EMA/CHMP/ICH/83812/2013)                                |

## Bibliography

### BOOKS, ARTICLES AND REPORTS

- Abbott, K., 'Public Private Partnership', in R. Wolfrum (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated February 2008, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.
- Abbott, K. & Snidal, D., 'Hard and Soft Law in International Governance', 54(3) *International Organization* (2000), pp. 421-456.
- Abbott, K. & Snidal, D., 'International 'Standards' and International Governance', 8(3) *Journal of European Public Policy* (2001), pp. 345-370.
- Abbott, K., Keohane, R., Moravcsik, A., Slaughter, A. & Snidal, D., 'The Concept of Legalization', 54(3) *International Organization* (2000), pp. 401-419.
- Abraham, J., 'The Pharmaceutical Industry as a Political Player', 360(9344) *The Lancet* (2002), pp. 1498-1502.
- Abraham, J. & Lewis, G., *Regulating Medicines in Europe: Competition, Expertise and Public Health* (London: Routledge, 2000).
- Abraham, J. & Reed, T., 'Trading Risks For Markets: The International Harmonization of Pharmaceuticals Regulation', 1(3) *Health, Risk and Society* (2001), pp. 113-128.
- Abraham, J. & Reed, T., 'Progress, Innovation and Regulatory Science in Drug Development: The Politics of International Standard-Setting', 32(3) *Social Studies of Science* (2002), pp. 337-369.
- Alemanno, A., 'The Shaping of European Risk Regulation by Community Courts', Jean Monnet Working Paper 18/2008, (2008).
- Alemanno, A., 'A Meeting of Minds on Impact-Assessment – When Ex Ante Evaluation Meets Ex Post Judicial Control', 17(3) *European Public Law* (2011), pp. 485-505.
- Alemanno, A., 'Regulating the European Risk Society', in Alemanno, A., den Butter, F., Nijsen, A. & Torriti, J. (Eds.), *Better Business Regulation in a Risk Society* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. 37-56.
- Alemanno, A., 'Unpacking the Principle of Openness in EU Law: Transparency, Participation and Democracy', 39(1) *European Law Review* (2014), pp. 72-90.
- Aman, A., 'The Limits of Globalization and the Future of Administrative Law: Government to Governance', 8(2) *Indiana Journal of Global Legal Studies* (2001), pp. 379-400.
- Archer, C., *International Organizations*, 3<sup>rd</sup> Edition, (London/New York: Routledge, 2001).
- Arnold, R., 'Objectives and Preparation of the Conference and the Role of the Workshops', in D'Arcy, P. & Harron, D. (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992), pp. 7-11.
- Arnulf, A., 'Private Applicants and the Action for Annulment since Codorniu', 38(7) *Common Market Law Review* (2001), pp. 7-52.
- Augier de Crémiers, F., 'The Birth of ICH E3 and How it Led to the CTD', 3(2) *Drug Information Association Global Forum* (2011), pp. 19-20.
- Aust, A., *Handbook of International Law*, 2<sup>nd</sup> Edition, (Cambridge: Cambridge University Press, 2010).
- Aziz, D., 'Global Public-Private Partnerships in International Law', 2(2) *Asian Journal of International Law* (2012), pp. 339-374.
- Bach, D., & Newman, A., 'The European Regulatory State and Global Public Policy: Micro-institutions, Macro-influence', 14(6) *Journal of European Public Policy* (2007), pp. 827-846.

- Bach, D. & Newman, A., 'Governing Lipitor and Listerine: The Domestic Roots of International Pharmaceutical and Cosmetics Regulation', IE Business School Working Paper, WP08-17, 11 March 2008.
- Bahri, P. & Tsintis, P., 'Pharmacovigilance-related Topics at the Level of the International Conference on Harmonisation (ICH)', 14(6) *Pharmacoepidemiology and Drug Safety* (2005), pp. 377-387.
- Baldwin, R. & Cave, M., *Understanding Regulation* (Oxford: Oxford University Press, 1999).
- Baldwin, J. & Davis, G., 'Empirical Research in Law', in Cane, P. & Tushnet, M. (Eds.), *The Oxford Handbook of Legal Studies* (Oxford: Oxford University Press, 2003), pp. 880-900.
- Bangemann, M., 'Welcome Address by Mr Martin Bangemann', in P. D'Arcy & D. Harron (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992), pp. 1-5.
- Bast, J., 'Internationalisierung und De-Internationalisierung der Migrationsverwaltung', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 279-312.
- Batory, A., 'Uploading as Political Strategy: the European Parliament and the Hungarian Media Law Debate', 30(2) *East European Politics* (2014), pp. 230-245.
- Baxter, R., 'International Law in "Her Infinite Variety"', 29(4) *International and Comparative Law Quarterly* (1980), pp. 549-566.
- Beck, U., *Risk Society: Towards a New Modernity* (London: Sage, 1992).
- Berman, A., 'The Public-Private Nature of Harmonization Networks', CTEI Working Paper, CTEI-2011-06, (2011a).
- Berman, A., 'The Role of Domestic Administrative Law in the Accountability of Transnational Regulatory Networks', CTEI Working Paper, CTEI-2011-08, (2011b)
- Berman, A., 'The Distributional Effects of Transnational Pharmaceutical Regulation', CTEI Working Paper, CTEI-2012-01, (2012a).
- Berman, A., 'Public-Private Harmonization Networks: The Case of the International Conference on Harmonization (ICH)', in Cassese, S., Carotti, B., Casini, L., Cavalieri, E. & MacDonald, E. (Eds.), *Global Administrative Law: The Casebook*, 3<sup>rd</sup> Edition (2012b), pp. 228-234, available via: <http://www.irpa.eu/wp-content/uploads/2012/08/The-Casebook-Chapter-1.pdf>, last accessed: 3 April 2017.
- Berman, A., 'Informal International Lawmaking in Medical Products Regulation', in Berman, A., Duquet, S., Pauwelyn, J., Wessel, R. & Wouters, J. (Eds.), *Informal International Lawmaking: Case Studies* (The Hague: Torkel Opsahl Academic Publishers, 2012c), pp. 353-393.
- Bevilaqua, D., 'The Codex Alimentarius Commission and its Influence on European and National Food Policy', 1(1) *European Food and Feed Law Review* (2006), pp. 3-14.
- Bignami, F., 'Three Generations of Participation Rights before the European Commission', 68(1) *Law and Contemporary Problems* (2004), pp. 61-83.
- Black, J., 'Critical Reflections on Regulation', Centre for Analysis of Risk and Regulation, CARR Discussion Papers DP 4, London School of Economics and Political Science, London, UK, (2002).
- Black, J., 'Constructing and Contesting Legitimacy and Accountability in Polycentric Regulatory Regimes', 2(2) *Regulation & Governance* (2008), pp. 137-164.
- Black, J., 'The Role of Risk in Regulatory Processes', in Baldwin, R., Cave, M. & Lodge, M. (Eds.), *The Oxford Handbook of Regulation* (Oxford: Oxford University Press, 2010), pp. 302-348.
- Blichner, L. & Molander, A., 'Mapping Juridification', 14(1) *European Law Journal* (2008), pp. 36-54.

- Bodansky, D., 'Legitimacy in International Law and International Relations', in Dunoff, J. & Pollack, M. (Eds.), *Interdisciplinary Perspectives on International Law and International Relations – The State of the Art* (Cambridge: Cambridge University Press, 2013), pp. 321-341.
- Borrás, S., 'Three Tensions in the Governance of Science and Technology', in D. Levi-Faur (Ed.), *The Oxford Handbook of Governance* (Oxford: Oxford University Press, 2012), pp.429-440.
- Borrás, S, Koutalakis, C. & Wendler, F., 'European Agencies and Input Legitimacy: EFSA, EMeA and EPO in the Post-Delegation Phase', 29(5) *Journal of European Integration* (2007), pp. 583-600.
- Börzel, T., 'Organizing Babylon – On the Different Conceptions of Policy Networks', 76(2) *Public Administration* (1998), pp. 253-273.
- Börzel, T. & Risse, T., 'Public-Private Partnerships: Effective and Legitimate Tools of International Governance?', in Grande, E. & Pauly, L. (Eds.), *Complex Sovereignty: On the Reconstruction of Political Authority in the 21st Century* (Toronto: University of Toronto Press, 2007), pp. 195-216.
- Bothe, M., 'Legal and Non-Legal Norms – A Meaningful Distinction in International Relations?', 11(65) *Netherlands Yearbook of International Law* (1980), pp. 65-95.
- Bouder, F., 'Handling Pharmaceutical Risks in Post-Trust Society – Science-based Decision Making under Strain?', in Van Asselt, M., Everson, M. & Vos, E. (Eds.), *Trade, Health and the Environment – The European Union Put to the Test* (Oxon/New York: Routledge/Earthscan, 2014), pp. 91-112.
- Bovens, M., 'Analysing and Assessing Accountability: A Conceptual Framework', 13(4) *European Law Journal* (2007), pp. 447-468.
- Bovens, M., Curtin, D. & 't Hart, P., 'Studying the Real World of EU Accountability: Framework and Design', in Bovens, M., Curtin, D. & 't Hart, P. (Eds.), *The Real World of EU Accountability – What Deficit?* (Oxford: Oxford University Press, 2010), pp. 31-62.
- Boyle, A., 'Some Reflections on the Relationship of Treaties and Soft Law', 48(4) *International and Comparative Law Quarterly* (1999), pp. 901-913.
- Bretherton, C. & Vogler, J., *The European Union as Global Actor*, 2<sup>nd</sup> Edition, (Oxon/New York: Routledge, 2006).
- Brüggenmeier, G., Falke, J., Joerges, C. & Micklitz, H. (Eds.), 'Special Issue: European Product Safety, Completion of the Internal Market and the New Approach to Technical Harmonisation and Standards – Reissued', 6(2) *Hanse Law Review* (2010).
- Buchanan, A. & Keohane, R., 'The Legitimacy of Global Governance Institutions', 20(4) *Ethics and International Affairs* (2006), pp. 405-437.
- Burci, G., 'Public/Private Partnerships in the Public Health Sector', 6(2) *International Organizations Law Review* (2009), pp. 359-382.
- Burgi, M., '§18 Rechtsregime', in Hoffmann-Riem, W., Schmidt-Aßmann, E. & Voßkuhle, A. (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 1257-1320.
- Busuioac, M., *European Agencies: Law and Practice of Accountability* (Oxford: Oxford University Press, 2013).
- Cafaggi, F., 'Rethinking Private Regulation in the European Regulatory Space', European University Institute Department of Law, EUI Working Papers Law No. 2006/13, (2006).
- Cafaggi, F. & Renda, A., 'Public and Private Regulation – Mapping the Labyrinth', Centre for European Policy Studies, CEPS Working Document No. 370, (October 2012).
- Carter, C. & Scott, A., 'Legitimacy and Governance beyond the European Nation State: Conceptualizing Governance in the European Union', 4(4) *European Law Journal* (1998), pp. 429-445.
- Casini, L., 'Global Hybrid Public-Private Bodies: The World Anti-Doping Agency (WADA)', 6(2) *International Organizations Law Review* (2009), pp. 421-446.

- Casini, L., “‘Down the Rabbit Hole’: The Projection of the Public/Private Distinction Beyond the State’, New York University School of Law, Jean Monnet Working Paper No. 8/2013, (2013).
- Casini, L., ‘Beyond drip-painting? Ten Years of GAL and the Mergence of a Global Administration’, 13(2) *International Journal of Constitutional Law* (2015), pp. 473-477.
- Cassese, S., ‘Administrative Law without the State? The Challenge of Global Regulation’, 37(4) *International Law and Politics* (2005), pp. 663-694.
- Cassese, S., ‘Global Administrative Law: The State of the Art’, 13(2) *International Journal of Constitutional Law* (2015), pp. 465-468.
- Cassese, S. (Ed.), *Research Handbook on Global Administrative Law* (Cheltenham: Edward Elgar, 2016).
- Castle, G. & Kelly, B., ‘Global Harmonization Is Not All That Global: Divergent Approaches in Drug Safety’, 63(3) *Food and Drug Law Journal* (2008) pp. 601-622.
- Cecchini, P., *The European challenge 1992 – Benefits of a Single Market* (Aldershot: Wildwood House, 1988).
- Charnovitz S., ‘International Standards and the WTO’, GW Law Faculty Publications & Other Works, Paper 394, (2005).
- Chesterman, S., ‘Rule of Law’, in Wolfrum, R. (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated July 2007, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.
- Chalmers, D., *European Union Public Law: Text and Materials*, 2<sup>nd</sup> Edition, (Cambridge: Cambridge University Press, 2010).
- Chamon, M., ‘EU Agencies in between Meroni and Romano or the Devil and the Deep Blue Sea’, 48(4) *Common Market Law Review* (2011), pp. 1055-1075.
- Chamon, M., *European Agencies – Legal and Political Limits to the Transformation of the EU Administration* (Oxford: Oxford University Press, 2016).
- Chinkin, C., ‘The Challenge of Soft Law: Development and Change in International Law’, 38(4) *International and Comparative Law Quarterly* (1989), pp. 850-866.
- Chiti, E. ‘The Emergence of a Community Administration: The Case of European Agencies’, 37(2) *Common Market Law Review* (2000), pp. 309-343.
- Chiti, E., ‘EU and Global Administrative Organizations’, in Chiti, E. & Mattarella, B. (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer 2011), pp. 13-39.
- Chiti, E., ‘European Agencies’ Rulemaking: Powers, Procedures and Assessment’, 19(1) *European Law Journal* (2013), pp. 93-110.
- Chiti, E., & Mattarella, B., (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer, 2011a).
- Chiti, E., & Mattarella, B., ‘Introduction: The Relationship Between Global Administrative Law and EU Administrative Law’, in Chiti, E. & Mattarella, B. (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer 2011b), pp. 1-10.
- Cini, M., ‘The Soft Law Approach: Commission Rule-making in the EU’s State Aid Regime’, 8(2) *Journal of European Public Policy* (2001), pp. 192-207.
- Clarke, L., ‘The Exercise of Public Power over Global Health through Public-Private Partnerships and the Question of Responsibility under International Law’, 105 *Proceedings of the Annual Meeting of the American Society of International Law* (2011), pp. 96-100.
- Coman-Kund, F., *European Union Agencies as Global Actors – A Legal Study of the European Aviation Safety Agency, Frontex and Europol* (Maastricht: Universitaire Pers Maastricht, 2015).
- Connolly, J., ‘Europeanization, Uploading and Downloading – The Case of Defra and Avian Influenza’, 23(1) *Public Policy and Administration* (2008), pp. 7-25.

- Contrera, J., 'The Food and Drug Administration and the International Conference on Harmonisation: How Harmonious Will International Pharmaceutical Regulation Become?', 8(4) *The Administrative Law Journal* (1994-1995), pp. 927-960.
- Craig, P., 'Legality, Standing and Substantive Review in Community Law', 14(4) *Oxford Journal of Legal Studies* (1994), pp. 507-537.
- Craig, P., *Administrative Law*, 7<sup>th</sup> Edition (London: Thomson Sweet & Maxwell, 2003).
- Craig, P., 'Delegated Acts, Implementing Acts and the New Comitology Regulation', 36(5) *European Law Review* (2011), pp. 671-687.
- Craig, P., *EU Administrative Law* (Oxford: Oxford University Press, 2012).
- Craig, P., 'A General Law on Administrative Procedure, Legislative Competence and Judicial Competence', 19(3) *European Public Law* (2013), pp. 503-524.
- Cremona, M., 'The Union as Global Actor: Roles, Models and Identity', 41(2) *Common Market Law Review* (2004), pp. 553-573.
- Cremona, M., 'External Relations and External Competence of the European Union: The Emergence of an Integrated Policy', in Craig, P. & de Búrca, G. (Eds.), *The Evolution of EU Law*, 2<sup>nd</sup> Edition (Oxford: Oxford University Press, 2011), pp. 217-268.
- Cremona, M., 'Expanding the Internal Market: An External Regulatory Policy for the EU?', in Van Vooren, B., Blockmans, S. & Wouters, J. (Eds.), *The EU's Role in Global Governance – The Legal Dimension* (Oxford: Oxford University Press, 2013), pp. 162-177.
- Curtin, D., 'Delegation to EU Non- Majoritarian Agencies and Emerging Practices of Public Accountability', in Geradin, D., Muñoz, R. & Petit, N. (Eds.), *Regulation Through Agencies in the EU: A New Paradigm of European Governance* (Cheltenham: Edward Elgar, 2006), pp. 88-119.
- Curtin, D., *Executive Power of the European Union – Law, Practice and the Living Constitution* (Oxford: Oxford University Press, 2009).
- Curtin, D. & Eckes, C., 'The Kadi Case: Mapping the Boundaries between the Executive and the Judiciary in Europe', 5(2) *International Organizations Law Review* (2008), pp. 365-369.
- Curtin, D. & Meijer, A., 'Does Transparency Strengthen Legitimacy?', 11(2) *Information Policy* (2006), pp. 109-122.
- Curtin, D., & Nollkaemper, A., 'Conceptualizing Accountability in International and European Law', 37 *Netherlands Yearbook of International Law* (2006), pp. 3-20.
- Curtin, D. & Senden, L., 'Public Accountability of Transnational Private Regulation: Chimera or Reality?', 38(1) *Journal of Law and Society* (2011), pp. 163-188.
- Curtin, D., Hofmann, H. & Mendes, J., 'Constitutionalising EU Executive Rule-Making Procedures: A Research Agenda', 19(1) *European Law Journal* (2013), pp. 1-21.
- Cutler, C., 'The Legitimacy of Private Transnational Governance: Experts and the Transnational Market for Force', 8(1) *Socio-Economic Review* (2010), pp. 157-185.
- Cutler, C., Haufler, V. & Porter, T. (Eds.), *Private Authority and International Affairs* (Albany: State University of New York Press, 1995).
- Dagron, S., 'Global Harmonization through Public-Private Partnership: The Case of Pharmaceuticals', Istituto di Ricerche sulla Pubblica Amministrazione, Global Administrative Law Working Papers, IRPA GAL Working Paper 2012/2, (2012).
- Dahl, R., 'Can International Organizations be Democratic? A Skeptic's View', in Shapiro, I. & Hacker-Cordón, C. (Eds.), *Democracy's Edges* (Cambridge: Cambridge University Press, 1999), pp. 19-36.
- Dann, P. & von Engelhardt, M., 'Legal Approaches to Global Governance and Accountability: Informal Lawmaking, International Public Authority, and Global Administrative Law Compared', in Pauwelyn, J., Wessel, R. & Wouters, J. (Eds.), *Informal International Law-Making* (Oxford: Oxford University Press, 2012), pp. 106-123.

- D'Arcy, P. & Harron, D. (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992).
- Dawson, M., 'Three Waves of New Governance in the European Union', 36(2) *European Law Review* (2011a), pp. 208-225.
- Dawson, M., *New Governance and the transformation of European Law: Coordinating EU Social Law and Policy* (Cambridge: Cambridge University Press, 2011b).
- de Búrca, G., 'Developing Democracy Beyond the State', 46(2) *Columbia Journal of Transnational Law* (2008), pp. 221- 278.
- de Búrca, G., 'The European Court of Justice and the International Legal Order After Kadi', 51(1) *Harvard International Law Journal* (2010), pp. 1-49.
- de Búrca, G. & Scott, J., 'Introduction: New Governance, Law and Constitutionalism', in de Búrca, G. & Scott, J. (Eds.), *Law and New Governance in the EU and the US* (Oxford: Hart Publishing, 2006), pp. 1-12.
- Dehousse, R., 'Regulation by Networks in the European Community: the Role of European Agencies', 4(2) *Journal of European Public Policy* (1997), pp. 246-261.
- Dehousse, R. 'Delegation of Powers in the European Union: The Need for Multi-principals Model', 31(4) *West European Politics* (2008), pp. 789-805.
- Derderer, H., *Korporative Staatsgewalt – Integration privat organisierter Interessen in die Ausübung von Staatsfunktionen. Zugleich eine Rekonstruktion der Legitimationsdogmatik* (Tübingen: Mohr Siebeck, 2004).
- Devaux, C., 'The Experts in the Elaboration of the Cape Town Convention: Between Authority and Legitimacy', 19(6) *European Law Journal* (2013), pp. 843-863.
- Dilling, O., Herberg, M. & Winter, G., 'Introduction – Exploring Transnational Administrative Rule-Making', in Dilling, O., Herberg, M. & Winter, G. (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 1-19.
- Dixon, M., *Textbook on International Law*, 5<sup>th</sup> Edition (Oxford: Oxford University Press, 2005).
- Doi, O., 'Role and Public Health Responsibilities of the Authorities', in D'Arcy, P. & Harron, D. (Eds.), *Proceedings of the First International Conference on Harmonisation – Brussels 1991* (Belfast: The Queen's University Belfast, 1992), pp. 18-26.
- Dorbeck-Jung, B., 'Challenges to the Legitimacy of International Regulation: The Case of Pharmaceuticals Standardisation', in Føllesdal, A., Wessel, R. & Wouters, J. (Eds.), *Multilevel Regulation and the EU: The Interplay between Global, European and National Normative Processes* (Leiden/Boston: Martinus Nijhoff Publishers, 2008), pp. 51-71.
- Dürner, W., 'Internationales Umweltverwaltungsrecht', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 121-164.
- Eckes, C., 'International Law as Law of the EU: The Role of the European Court of Justice', in Canizzaro, E., Palchetti, P. & Wessel, R. (Eds.), *International Law as Law of the European Union* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), pp. 353-377.
- Eeckhout, P., *EU External Relations Law*, 2<sup>nd</sup> Edition, (Oxford: Oxford University Press, 2011).
- EFPIA, 'The Pharmaceutical Industry in Figures – Key Data 2016', available via: <http://www.efpia.eu/uploads/Modules/Documents/the-pharmaceutical-industry-in-figures-2016.pdf>, last accessed: 3 April 2017.
- Ehnert, T., *Regulating the Invisible – A Critical Analysis of the EU's Approach to Nanotechnologies* (Maastricht: Universitaire Pers Maastricht, 2015).
- Eichler, H., Bloechel-Daum, B., Brasseur, D., Breckenridge, A., Leufkens, H., Raine, J., Salmonson, T., Schneider, C. & Rasi, G., 'The Risks of Risk Aversion in Drug Regulation', 12(12) *Nature Reviews Drug Discovery* (2013), pp. 907-916.

- Eifert, M., '§19 Regulierungsstrategien', in Hoffmann-Riem, W., Schmidt-Aßmann, E. & Voßkuhle, A. (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 1319-1394.
- Esty, D., 'Good Governance at the Supranational Scale: Globalizing Administrative Law', 115(7) *Yale Law Journal* (2005-2006), pp. 1490-1562.
- Everson, M. & Vos, E., 'European Risk Governance in a Global Context', in Vos, E. (Ed.), *European Risk Governance -Its Science, its Inclusiveness and its Effectiveness*, Connex Report Series No. 6 (2008), pp. 7-36.
- Everson, M. & Vos, E., 'The Scientification of Politics and the Politicization of Science', in Everson, M. & Vos, E. (Eds.), *Uncertain Risks Regulated* (Oxon: Routledge/Cavendish, 2009), pp. 1-18.
- Everson, M., Monda, C. & Vos, E. (Eds.), *European Agencies In Between Institutions and Member States* (Alphen aan den Rijn: Kluwer Law International, 2014).
- Feick, J., 'Learning and Interest Accommodation in Policy and Institutional Change: EC Risk Regulation in the Pharmaceuticals Sector', ESCR Centre for Analysis of Risk and Regulation (CARR) Discussion Paper 25, (January 2005).
- Feldschreiber, P. (Ed.), *The Law and Regulation of Medicines* (Oxford: Oxford University Press, 2008).
- Fink, M., 'Frontex Working Agreements: Legitimacy and Human Rights Concerns Regarding "Technical Relationships"', 28(75) *Utrecht Journal of International and European Law* (2012), pp. 20-35.
- Fisher, E., 'Drowning by Numbers: Standard-Setting in Risk Regulation and the Pursuit of Accountable Public Administration', 20(1) *Oxford Journal of Legal Studies* (2000), pp. 109-130.
- Fisher, E., 'Unpacking the Toolbox: Or Why the Public/Private Divide is Important in EC Environmental Law', Florida State University College of Law – Public Law and Legal Theory Working Paper No. 35, (August 2001).
- Fisher, E., 'The European Union in the Age of Accountability', 24(3) *Oxford Journal of Legal Studies* (2004), pp. 495-515.
- Fisher, E., *Risk Regulation and Administrative Constitutionalism* (Oxford/Portland: Hart Publishing, 2010).
- Føllesdal, A., Wessel, R. & Wouters, J. (Eds.), *Multilevel Regulation and the EU: The Interplay between Global, European and National Normative Processes* (Leiden: Koninklijke Brill, 2008).
- Gehring, T. & Krapohl, S., 'Supranational Regulatory Agencies between Independence and Control: the EMEA and the Authorisation of Pharmaceuticals in the European Single Market', 14(2) *Journal of European Public Policy* (2007), pp. 208-226.
- Gemkow, T. & Zürn, M., 'Constraining International Authority through the Rule of Law: Legitimatory Potential and Political Dynamics', in Zürn, M., Nollkaemper, A. & Peerboom, R. (Eds.), *Rule of Law Dynamics – In an Era of International and Transnational Governance* (Cambridge: Cambridge University Press, 2012), pp. 68-89.
- Geradin, D., Muñoz, R. & Petit, N. (Eds.), *Regulation through Agencies in the EU – A New Paradigm of European Governance* (Cheltenham: Edward Elgar, 2006).
- Goldmann, M., 'Inside Relative Normativity: From Sources to Standard Instruments for the Exercise of International Public Authority', in von Bogdandy, A., Wolfrum, R., von Bernstorff, J., Dann, P. & Goldmann, M. (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 661-711.
- Goldmann, M., *Internationale öffentliche Gewalt – Handlungsformen internationaler Institutionen im Zeitalter der Globalisierung* (Heidelberg: Springer, 2015).

- Goldmann, M., 'A Matter of Perspective: Global Governance and the Distinction between Public and Private Authority (and Not Law)', 5(1) *Global Constitutionalism* (2016), pp. 48-84.
- Grant, R. & Keohane, R., 'Accountability and Abuses of Power in World Politics', 99(1) *American Political Science Review* (2005), pp. 29-43.
- Griller, S. & Orator, A., 'Everything under Control? The "Way Forward" for European Agencies in the Footsteps of the Meroni Doctrine', 35(1) *European Law Review* (2010), pp. 3-35.
- Groenleer, M., *The Autonomy of European Union Agencies – A Comparative Study of Institutional Developments* (Delft: Eburon, 2009).
- Groenleer, M., 'Linking Up Levels of Governance: Agencies of the European Union and International Institutions', in Costa, O. & Joergensen, K. (Eds.), *The Influence of International Institutions on the European Union: When Multilateralism Hits Brussels* (Basingstoke: Palgrave Macmillan, 2012), pp. 135-154.
- Groenleer, M. & Gabbi, S., 'Regulatory Agencies of the European Union as International Actors: Legal Framework, Development over Time and Strategic Motives in the Case of the European Food Safety Authority', 4(4) *European Journal of Risk Regulation* (2013), pp. 479-492.
- Haas, P., 'Introduction: Epistemic Communities and International Policy Coordination', 46(1) *International Organization* (1992), pp. 1-35.
- Habermas, J., *The Theory of Communicative Action – Volume 2* (Boston: Beacon Press, 1987).
- Habermas, J., *Between Facts and Norms – Contributions to a Discourse Theory of Law and Democracy* (Cambridge, Massachusetts: MIT Press, 1996).
- Habermas, J., 'Die Postnationale Konstellation und die Zukunft der Demokratie', in Habermas, J., *Die Postnationale Konstellation – Politische Essays* (Frankfurt am Main: Suhrkamp Verlag, 1998), pp. 91-169.
- Hachez, N. & Wouters, J., 'A Glimpse at the Democratic Legitimacy of Private Standards: Assessing the Public Accountability of Global G.A.P.', 14(3) *Journal of International Economic Law* (2011), pp. 677-710.
- Hancher, L., *Regulating for Competition – Government, Law and the Pharmaceutical Industry in the United Kingdom and France* (Alblasserdam: Haveka, 1989).
- Hancher, L., 'Creating the Internal Market for Pharmaceutical Medicines – An Echternach Jumping Procession?', 28(4) *Common Market Law Review* (1991), pp. 821-853.
- Harlow, C., 'Towards a Theory of Access for the European Court of Justice', 12(1) *Yearbook of European Law* (1992), pp. 213-248.
- Harlow, C., 'Global Administrative Law: the Quest for Principles and Values', 17(1) *European Journal of International Law* (2006), pp. 187-214.
- Harlow, C., 'Composite Decision-Making and Accountability Networks: Some Deductions from a Saga', 32(1) *Yearbook of European Law* (2013), pp. 3-29.
- Herberg, M., 'Global Governance Networks in Action: The Development of Toxicological Test Methods at the OECD', in Dilling, O., Herberg, M. & Winter, G. (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 77-108.
- Héretier, A. & Rhodes, M. (Eds.), *New Modes of Governance in Europe: Governing in the Shadow of Hierarchy* (Basingstoke/New York: Palgrave Macmillan, 2010).
- Herwig, A., 'The Contribution of Global Administrative Law to Enhancing the Legitimacy of the Codex Alimentarius Commission', in Dilling, O., Herberg, M. & Winter, G. (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 171-212.

- Hodgkin, C., 'International Harmonisation – The Need for Transparency', 9(3) *International Journal of Risk & Safety in Medicine* (1996), pp. 195-199.
- Hofmann, H., 'Seven Challenges for EU Administrative Law', 2(2) *Review of European Administrative Law* (2009), pp. 37-59.
- Hofmann, H., 'Dealing with Trans-Territorial Executive Rule-Making', 78(3) *Missouri Law Review* (2013), pp. 423-442.
- Hofmann, H., 'Agencies in the European Regulatory Union', TARN Working Paper 5/2016, June 2016, available via: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=2804230](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2804230), last accessed: 3 April 2017.
- Hofmann, H. & Mihaescu, B., 'The Relation between the Charter's Fundamental Rights and the Unwritten General Principles of EU Law: Good Administration as the Test Case', 9(1) *European Constitutional Law Review* (2013), pp. 73-101.
- Hofmann, H., & Türk, A., 'An Introduction to EU Administrative Governance', in Hofmann, H. & Türk, A. (Eds.), *EU Administrative Governance* (Cheltenham/-Northampton: Edward Elgar, 2006), pp. 1-10.
- Hofmann, H., & Türk, A., 'Die Ausübung übertragener Normsetzungsbefugnisse durch die Europäische Kommission: Verfahrensrecht in einer neuen Dimension', 27(2) *Zeitschrift für Gesetzgebung* (2012), pp. 105-137.
- Hofmann, H., Rowe, G. & Türk, A., *Administrative Law and Policy of the European Union* (Oxford: Oxford University Press, 2011).
- Hofmann, H., Schneider, J. & Ziller, J., 'The Research Network on European Administrative Law's Project on EU Administrative Procedure – Its Concepts, Approaches and Results', 7(2) *Review of European Administrative Law* (2014), pp. 45-64.
- Hood, C., Rothstein, H. & Baldwin, R., *The Government of Risk: Understanding Risk Regulation Regimes* (Oxford: Oxford University Press, 2003).
- Howell, K., 'Uploading, Downloading and European Integration: Assessing the Europeanisation of UK Financial Services Regulation', 6(1) *Journal of International Banking Regulation* (2004), pp. 53-68.
- Howorth, J. 'The EU as a Global Actor: Grand Strategy for a Global Grand Bargain?', 48(3) *Journal of Common Market Studies* (2010), pp. 455-474.
- Hurd, I., 'Legitimacy and Authority in International Politics', 53(2) *International Organization* (1999), pp. 379-408.
- Jasanoff, S., 'Epistemic Subsidiarity – Coexistence, Cosmopolitanism, Constitutionalism', 4(2) *European Journal of Risk Regulation* (2013), pp. 133-141.
- Joerges, C., 'Law, Science and the Management of Risks to Health at the National, European and International Level: Stories on Baby Dummies, Mad Cows and Hormones in Beef', 7(1) *Columbia Journal of European Law* (2001), pp. 1-20.
- Joerges, C., Schepel, H. & Vos, E., 'The Law's Problems with the Involvement of Non-Governmental Actors in Europe's Legislative Processes: The Case of Standardisation under the "New Approach"', EU Working Paper Law No. 99/9, (October 1999).
- Jordan, D., 'International Regulatory Harmonization: A New Era in Prescription Drug Approval', 25(3) *Vanderbilt Journal of Transnational Law* (1992), pp. 471-507.
- Julliet, Y., 'CTD – A Tool for Global Development and Assessment', 3(2) *Drug Information Association Global Forum* (2011), pp. 25-26.
- Kaddous, C., 'Effects of International Agreements in the EU Legal Order', in Cremona, M. & de Witte, D. (Eds.), *EU Foreign Relations Law: Constitutional Fundamentals* (Oxford/Portland: Hart Publishing, 2008), pp. 291-312.
- Kadelbach, S., 'EU Administrative Law and the Law of the Europeanized Administration', in Joerges, C. & Dehousse, R. (Eds.), *Good Governance in Europe's Integrated Market* (Oxford: Oxford University Press, 2002), pp. 167-206.

- Kalberg, S. (Ed.), *Max Weber – Readings and Commentary on Modernity* (Malden/Oxford/Carlton: Blackwell, 2005).
- Kanusky, R., 'Pharmaceutical Harmonization: Standardizing Regulations among the United States, the European Economic Community, and Japan', 16(3) *Houston Journal of International Law* (1994), pp. 665-707.
- Katsikas, D., 'International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceutical Products', in Hale, T. & Held, D. (Eds.), *Handbook of Transnational Governance – Institutions & Innovations* (Cambridge: Polity Press, 2011), pp. 88-94.
- Kaul, I., 'Exploring the Space between Markets and States: Global Public-Private Partnerships', in Kaul, I. & Conceicao, P. (Eds.), *The New Public Finance: Responding to Global Challenges* (Oxford/New York: Oxford University Press, 2006), pp. 219-268.
- Keohane, R., 'Global Governance and Legitimacy', 18(1) *Review of International Political Economy* (2011), pp. 99-109.
- Keohane, R. & Nye, J., 'Transgovernmental Relations and International Organizations', 27(1) *World Politics* (1974), pp. 39-62.
- Kerwer, D., 'Standardising as Governance: The case of credit rating agencies', MPI Collective Goods Preprint, No. 2001/3, (2001).
- Kerwer, D., 'Rules that Many Use: Standards and Global Regulation', 18(4) *Governance* (2005), pp. 611-632.
- Kica, E. & Bowman, D., 'Transnational Governance Arrangements: Legitimate Alternatives to Regulating Nanotechnologies?', 7(1) *NanoEthics* (2013), pp. 69-82.
- Kidd, D., 'The International Conference on Harmonization of Pharmaceutical Regulations, the European Medicines Evaluation Agency, and the FDA: Who's Zooming Who?', 4(1) *Indiana Journal of Global Legal Studies* (1996), pp. 183-206.
- Kingsbury, B., 'The Administrative Law Frontier in Global Governance', 99 *Proceedings of the Annual Meeting of the American Society of International Law* (2005), pp. 143-153.
- Kingsbury, B. & Casini, L., 'Global Administrative Law Dimensions of International Organizations Law', 6(2) *International Organizations Law Review* (2009), pp. 319-358.
- Kingsbury, B. & Stewart, R., 'Legitimacy and Accountability in Global Regulatory Governance: The Emerging Global Administrative Law and the Design and Operation of Administrative Tribunals Of International Organizations', in Papanikolaou, K. & Hiskaki, M. (Eds.), *International Administrative Tribunals in a Changing World* (London: Esperia Publications Ltd., 2008), pp. 193-220.
- Kingsbury, B., Krisch, N. & Stewart, R., 'The Emergence of Global Administrative Law', 68(3&4) *Law and Contemporary Problems* (2005), pp. 15-62.
- Klabbers, J., 'The Redundancy of Soft Law', 65(2) *Nordic Journal of International Law* (1996), pp. 167-182.
- Klabbers, J., 'The Undesirability of Soft Law', 67(4) *Nordic Journal of International Law* (1998), pp. 381-391.
- Klabbers, J., *An Introduction to International Institutional Law*, 2<sup>nd</sup> Edition, (Cambridge: Cambridge University Press, 2002).
- Knauff, M., *Der Regelungsverbund: Recht und Soft Law im Mehrebenensystem* (Tübingen: Mohr Siebeck, 2010).
- Koehlin, L. & Calland, R., 'Standard Setting at the Cutting Edge: an Evidence-Based Typology for Multi-stakeholder Initiatives', in Peters, A., Koehlin, L., Förster, T. & Fenner Zinkernagel, G. (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009), pp. 1-32.
- Kohler-Koch, B. & Eising, R. (Eds.), *The Transformation of Governance in the European Union* (London: Routledge, 1999).

- Kohler-Koch, B. & Quittkat, C. (Eds.), *De-Mystification of Participatory Democracy* (Oxford: Oxford University Press, 2013).
- Kooiman, J. (Ed.), *Modern Governance: New Government – Society Interactions* (London: Sage, 1993).
- Korkea-aho, E., 'Better Judicial Review? EU Courts and the Smart Regulation Agenda in Implementing Chemical Regulation', 6(3) *Legisprudence* (2012), pp. 397-423.
- Korkea-aho, E., 'Legal Interpretation of EU Framework Directives: a Soft Law Approach', 40(1) *European Law Review* (2015), pp. 70-88.
- Koutrakos, P., *EU International Relations Law*, 2<sup>nd</sup> Edition (Oxford/Portland: Hart Publishing, 2015).
- Krajewski, M., 'International Organizations or Institutions, Democratic Legitimacy', in Wolfrum, R. (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated May 2008, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.
- Krapohl, S., 'Thalidomide, BSE and the Single Market: An Historical-Institutionalist Approach to Regulatory Regimes in the EU', 46(1) *European Journal of Political Research* (2007), pp. 25-46.
- Krisch, N., 'The Pluralism of Global Administrative Law', 17(1) *European Journal of International Law* (2006), pp. 247-278.
- Krisch, N., 'Das Migrationsrecht und die Internationalisierung des Verwaltungsrechts', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 313-318.
- Krisch, N., & Kingsbury, B., 'Introduction: Global Governance and Global Administrative Law in the International Legal Order', 17(1) *The European Journal of International Law* (2006), pp. 1-13.
- Kudryavtsev, A., *Private-Sector Standards as Technical Barriers in International Trade in Goods: In Search of WTO Disciplines* (Oisterwijk: Wolf Legal Publishers, 2015).
- Kuhnert, B., 'ICH at 20: An Overview', 3(2) *Drug Information Association Global Forum* (2011), pp. 17-18.
- Kumm, M., 'The Legitimacy of International Law: A Constitutionalist Framework of Analysis', 15(5) *European Journal of International Law* (2004), pp. 907-931.
- Ladeur, K., 'Towards a Legal Theory of Supranationality – The Viability of the Network Concept', 3(1) *European Law Journal* (1997), pp. 3-54.
- Ladeur, K., 'Die Internationalisierung des Verwaltungsrechts: Versuch einer Synthese', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 375-394.
- Lee, J., 'What is Past is Prologue: The International Conference on Harmonization and Lessons Learned from European Drug Regulations Harmonization', 26(1) *University of Pennsylvania Journal of International Economic Law* (2005), pp. 151-191.
- Lezotte, P., *International Cooperation, Convergence and Harmonization of Pharmaceutical Regulations – A Global Perspective* (Oxford/San Diego: Academic Press Elsevier, 2014).
- Lin, C., 'Public-Private Regime Interactions in Global Food Safety Governance', 69(2) *Food and Drug Law Journal* (2014), pp. 143-160.
- Lin, C., 'The European Food Safety Authority in Global Food Safety Governance: A Participant, a Benchmark, and a Model', in Alemanno, A. & Gabbi, S. (Eds.), *Foundations of EU Food Law and Policy* (Farnham/Burlington: Ashgate, 2014), pp. 347-362.
- Linder, S. & Vaillancourt Rosenau, P., 'Mapping the Terrain of the Public-Private Partnership', in Vaillancourt Rosenau, P. (Ed.), *Public-Private Policy Partnerships* (Cambridge, MA: MIT Press, 2000), pp. 1-19.

- Lindstrom, L., 'ICH Guideline Implementation', in ICH, *The Value and Benefits of ICH to Drug Regulatory Authorities – Advancing Harmonization for Better Health* (2010), available via: <http://www.ich.org/ichnews/publications/browse/article/the-values-and-benefits-of-ich-to-industry.html>, last accessed: 3 April 2017, pp. 9-10.
- Lisman, J. & Lekkerkerker, J., 'Four Decades of European Medicines Regulation: What Have They Brought Us?', 17(1&2) *International Journal of Risk & Safety in Medicine* (2005), pp. 73-79.
- Livmore, M., 'Authority and Legitimacy of Global Governance: Deliberation, Institutional Differentiation, and the Codex Alimentarius', 81(2) *New York University Law Review* (2006), p. 766-801.
- Majone, G., 'Science and Trans-Science in Standard Setting', 9(1) *Science, Technology, & Human Values* (1984), pp. 15-22.
- Majone, G., 'The Rise of the Regulatory State in Europe', 17(3) *West European Politics* (1994), pp. 77-101.
- Majone, G., 'Europe's 'Democratic Deficit': The Question of Standards', 4(1) *European Law Journal* (1998), pp. 5-28.
- Makkai, T. & Braithwaite, J., 'In and Out the Revolving Door: Making Sense of Regulatory Capture', 12(1) *Journal of Public Policy* (1992), pp. 61-78.
- Marx, A., Maertens, M., Swinnen, J. & Wouters, J., *Private Standards And Global Governance – Economic, Legal and Political Perspectives* (Cheltenham: Edward Elgar Publishing Ltd., 2012).
- Masson-Matthee, M., *The Codex Alimentarius Commission and Its Standards* (The Hague: TMC Asser Press, 2007).
- Masson-Matthee, M., 'The Codex Alimentarius Commission and its Food Safety Measures in the Light of their New Status', in Everson, M. & Vos, E. (Eds.), *Uncertain Risks Regulated* (Oxon: Routledge/Cavendish, 2009), pp. 324-388.
- Mattli, W. & Büthe, T., 'Setting international standards: Technological Rationality or Primacy of Power?', 56(1) *World Politics* (2003), pp. 1-42.
- Mattli, W., 'The Politics and Economics of Institutional Standards Setting: An Introduction', 8(3) *Journal of European Public Policy* (2001), pp. 328-344.
- Mayntz, R., 'Legitimacy and Compliance in Transnational Governance', MPIfG Working Paper 10/5, (2010).
- Meidinger, E., 'The Administrative Law of Global Private-Public Regulation: the Case of Forestry', 17(1) *European Journal of International Law* (2006), pp. 47-87.
- Mendes, J., 'Administrative Law Beyond the State: Participation at the Intersection of Legal Systems', in Chiti, E. & Mattarella, B. (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer, 2011a), pp. 111-132.
- Mendes, J., *Participation in EU Rule-Making – A Rights-Based Approach* (Oxford: Oxford University Press, 2011b).
- Mendes, J., 'Participation and the Role of Law after Lisbon: A Legal View on Article 11 TEU', 48(6) *Common Market Law Review* (2011c), pp. 1849-1878.
- Mendes, J., 'EU Law and Global Regulatory Regimes: Hollowing Out Procedural Standards?', 10(4) *International Journal of Constitutional Law* (2012), pp. 988-1022.
- Mendes, J., 'Rule of Law and Participation: A Normative Analysis of Internationalized Rulemaking as Composite Procedures', 12(2) *International Journal of Constitutional Law* (2014), pp. 370-401.
- Mendez, M., 'The Legal Effect of Community Agreements: Maximalist Treaty Enforcement and Judicial Avoidance Techniques', 21(1) *The European Journal of International Law* (2010), pp. 83-104.
- Menon, A. & Weatherill, S., 'Transnational Legitimacy in a Globalising World: How the European Union Rescues its States', 31(3) *West European Politics* (2008), pp. 397-416.

- Meuwese, A., Schuurmans, Y. & Voermans, W., 'Towards a European Administrative Procedure Act', 2(2) *Review of European Administrative Law* (2009), pp. 3-35.
- Millstone, E. & van Zwanenberg, P., 'The Evolution of Food Safety Policy-Making Institutions in the UK, EU and Codex Alimentarius', 36(6) *Social Policy & Administration* (2002), pp. 593-609.
- Möllers, C., 'Transnationale Behördenkooperation – Verfassungs- und Völkerrechtliche Probleme Transnationaler Administrativer Standardsetzung', 65(2) *Zeitschrift für ausländisches öffentliches Recht und Völkerrecht* (2005a), pp. 351-389.
- Möllers, C., 'Netzwerk als Kategorien des Organisationsrechts – Zur Juristischen Beschreibung Dezentraler Steuerung', in Obbecke, J. (Ed.), *Nicht-normative Steuerung in Dezentralen Systemen* (Stuttgart: Franz Steiner Verlag, 2005), pp. 285-302.
- Möllers, C., 'European Governance: Meaning and Value of a Concept', 43(3) *Common Market Law Review* (2006), pp. 313-336.
- Möllers, C., 'Internationales Verwaltungsrecht – Eine Einführung in die Referenzanalyse', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 1-6.
- Möllers, C., 'Ten Years of Global Administrative Law', 13(2) *International Journal of Constitutional Law* (2015), pp. 469-472.
- Möllers, C. & Terhechte, J., '§40 Europäisches Verwaltungsrecht und Internationales Verwaltungsrecht', in Terhechte, J., (Ed.), *Verwaltungsrecht der Europäischen Union* (Baden-Baden: Nomos, 2011), pp. 1437-1452.
- Molzon, J., 'The International Conference on Harmonization Common Technical Document – Global Submission Format?', 60(3) *Food and Drug Law Journal* (2005), pp. 447-451.
- Molzon, J., 'The Value and Benefit of the International Conference on Harmonisation (ICH) to Drug Regulatory Authorities: Advancing Harmonization for Better Public Health', in van der Laan, J. & DeGeorge, J. (Eds.), *Global Approaches in Safety Testing – ICH Guidelines Explained* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. 23-28.
- Molzon, J., Giaquinto, A., Lindstrom, L., Tominaga, T., Ward, M., Doerr, P., Hunt, L. & Rago, L., 'The Value and Benefits of the International Conference on Harmonisation to Drug Regulatory Authorities: Advancing Harmonization for Better Public Health', 89(4) *Clinical Pharmacology & Therapeutics* (2011), pp. 503-512.
- Morais, H., 'The Quest for International Standards: Global Governance vs. Sovereignty', 50(4) *University of Kansas Law Review* (2001-2002), pp. 779-821.
- Moravcsik, A., 'In Defence of the 'Democratic Deficit': Reassessing Legitimacy in the European Union', 40(4) *Journal of Common Market Studies* (2002), pp. 603-624.
- Mossialos, E., Mrazek, M., & Walley, T., 'Regulating Pharmaceuticals in Europe: an Overview', in Mossialos, E., Mrazek, M. & Walley, T. (Eds.), *Regulating Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality* (Maidenhead: Open University Press, 2004), pp. 1-37.
- Mullard, A., 'Mediator Scandal Rocks French Medical Community', 377(9679) *The Lancet* (2011), pp. 890-892.
- Müller-Graff, P., 'Das "Soft Law" der Europäischen Organisationen', 1 *Europarecht* (2012), pp. 18-34.
- Nadvi, K. & Wältring, F., 'Making Sense of Global Standards', INEF Report Heft 58/2002 (2002).
- Nanz, P. & Steffek, J., 'Global Governance, Participation and the Public Sphere', 39(2) *Government and Opposition* (2004), pp. 314-335.
- National Institute for Public Health and the Environment, 'Minds Open – Sustainability of the European Regulatory System for Medicinal Products', RVIM-Report 2014-0033.

- Neumeyer, K., *Internationales Verwaltungsrecht – Vol. IV: Allgemeiner Teil* (Zürich/Leipzig: Verlag für Recht und Gesellschaft, 1936).
- Newman, A. & Zaring, D., 'Regulatory Networks: Power, Legitimacy, and Compliance', in Dunoff, J. & Pollack, M. (Eds.), *Interdisciplinary Perspectives of International Law and International Relations – The State of the Art* (Cambridge: Cambridge University Press, 2013), pp. 244-265.
- Orzack, L., Kaitin, K. & Lasagna, L., 'Pharmaceutical Regulation in the European Community: Barriers to Single Market Integration', 17(4) *Journal of Health Politics, Policy and Law* (1992), pp. 847-868.
- Ott, A., 'EU Regulatory Agencies in EU External Relations: Trapped in a Legal Minefield Between European and International Law', 13(4) *European Foreign Affairs Review* (2008), pp. 515-540.
- Ott, A., Vos, E. & Coman-Kund, F., 'European Agencies on the Global Scene: EU and International Law Perspectives', in Everson, M., Monda, C. & Vos, E. (Eds.), *European Agencies In Between Institutions And Member States* (Alphen aan den Rijn: Kluwer Law International, 2014), pp. 87-122.
- Papadopoulos, Y., 'Shifts in Governance: Problems of Legitimacy and Accountability – Synthesising Study of the NOW programme "Shifts in Governance"', Netherlands Organisation for Scientific Research, March 2011, The Hague.
- Parkins, M., 'Pharmacological Practices of Ancient Egypt', in Whitelaw, W. (Ed.), *The Proceedings of the 10th Annual History of Medicine Days, Calgary March 23rd and 24th 2001*, pp. 5-11, available via: <http://www.ucalgary.ca/uofc/Others/HOM/Dayspapers2001.pdf>, last accessed: 3 April 2017.
- Pauwelyn, J., 'Informal International Lawmaking: Mapping the Action and Testing Concepts of Accountability and Effectiveness', CTEI Working Papers, CTEI-2011-05, (2011).
- Pauwelyn, J., 'Informal International Lawmaking: Framing the Concept and Research Questions', in Pauwelyn, J., Wessel, R. & Wouters, J. (Eds.), *Informal International Lawmaking* (Oxford: Oxford University Press, 2012), pp. 13-34.
- Pereira, R., 'Why Would International Administrative Activity Be Any Less Legitimate? – A Study of the Codex Alimentarius Commission', in von Bogdandy, A., Wolfrum, R., von Bernstorff, J., Dann, P. & Goldmann, M. (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 541-571.
- Permanand, G., *EU Pharmaceutical Regulation: The Politics of Policy-Making* (Manchester: Manchester University Press, 2006).
- Permanand, G. & Altenstetter, C., 'The Politics of Pharmaceuticals in the European Union', in Mossialos, E., Mrazek, M. & Walley, T. (Eds.), *Regulating Pharmaceuticals in Europe: Striving for Efficiency, Equity and Quality* (Maidenhead: Open University Press, 2004), pp. 38-54.
- Peters, A., 'The Position of International Law Within the European Community Legal Order', 40 *German Yearbook of International Law* (1997), pp. 9-78.
- Peters, A. & Pagotto, I., 'Soft Law as a New Mode of Governance: A Legal Perspective', New Modes of Governance Project Paper 04/D11, (2006).
- Peters, A. & Peter, S., 'International Organizations: Between Technocracy and Democracy', in Fassbender, B. & Peters, A. (Eds.), *The Oxford Handbook of the History of International Law* (Oxford: Oxford University Press, 2012), pp. 170-197.
- Peters, A., Koechlin, L., Förster, T. & Fenner Zinkernagel, G. (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009).
- Peters, A., Koechlin, L. & Fenner Zinkernagel, G., 'Non-State Actors as Standard Setters: Framing the Issue in an Interdisciplinary Fashion', in Peters, A., Koechlin, L., Förster, T.

- & Fenner Zinkernagel, G. (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009), pp. 1-32.
- Poggi, G., *Weber – A Short Introduction* (Cambridge/Malden: Polity Press, 2008).
- Ponce Solé, J., 'The History of Legitimate Administration in Europe', in Ruffert, M., (Ed.), *Legitimacy in European Administrative Law: Reform and Reconstruction* (Groningen: European Law Publishing, 2011a), pp. 155-173.
- Ponce Solé, J., 'EU Law, Global Law and the Right to Good Administration', in Chiti, E. & Mattarella, B. (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer 2011b), pp. 133-145.
- Pound, R., 'Law in Books and Law in Action', 44(1) *American Law Review* (1910), pp. 12-44.
- Purnhagen, K., 'The Challenge of Globalization in Pharmaceutical Law – Is an International Drug Approval System Modeled after the European System Worth Considering?', 63(3) *Food and Drug Law Journal* (2008), pp. 623-645.
- Purnhagen, K., 'Competition of Agencies in European Pharmaceutical Law – Does It Exist, Is it Desirable and How to Handle it?', 1(3) *European Journal of Risk Regulation* (2010), pp. 227-238.
- Quack, S., 'Law, Expertise and Legitimacy in Transnational Economic Governance: An Introduction', 8(1) *Socio-Economic Review* (2010), pp. 3-16.
- Raustiala, K., 'The Architecture of International Cooperation: Transgovernmental Networks and the Future of International Law', 43(1) *Virginia Journal of International Law* (2002-2003), pp. 1-92.
- Raustiala, K., 'Form and Substance of International Agreements', 99(3) *The American Journal of International Law* (2005), pp. 581-614.
- Renn, O., *Risk Governance – Coping with Uncertainty in a Complex World* (London: Routledge, 2008).
- Research Network on European Administrative Law (ReNEUAL), 'Introduction to the ReNEUAL Model Rules/ Book I – General Provisions', 2014, available via: [http://www.reneual.eu/images/Home/BookI-general\\_provision\\_2014-09-03\\_individualized\\_final.pdf](http://www.reneual.eu/images/Home/BookI-general_provision_2014-09-03_individualized_final.pdf), last accessed: 3 April 2017.
- Research Network on European Administrative Law (ReNEUAL), 'ReNEUAL Model Rules on EU Administrative Procedure/ Book II – Administrative Rulemaking', 2014, available via: [http://www.reneual.eu/images/Home/BookII-AdministrativeRulemaking\\_individualized\\_final\\_2014\\_09\\_03.pdf](http://www.reneual.eu/images/Home/BookII-AdministrativeRulemaking_individualized_final_2014_09_03.pdf), last accessed: 3 April 2017.
- Rhodes, R., *Understanding Governance: Policy Networks, Reflexivity and Accountability* (Buckingham: Open University Press, 1997).
- Risse, T., 'Transnational Governance and Legitimacy', in Benz, A. & Papadopoulos, Y. (Eds.), *Governance and Democracy – Comparing National, European and International Experiences* (Oxon: Routledge, 2006), pp. 179-199.
- Rizzi, M., 'Simple, Safe and Transparent (?): Preliminary Reflections on the Proposal for a New EU Regulation of Clinical Trials', 4(4) *European Journal of Risk Regulation* (2013), pp. 534-538.
- Rockhold, F., 'Industry Perspectives on ICH guidelines', 21(19) *Statistics in Medicine* (2002), pp. 2949-2957.
- Röhl, H., 'Internationale Standardsetzung', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 319-343.
- Rosenau, J., 'Governance, Order and Change in World Politics', in Rosenau, J. & Czempiel, E. (Eds.), *Governance without Government: Order and Change in World Politics* (Cambridge: Cambridge University Press, 1992), pp. 1-29.

- Rosenau, J. & Czempiel, E. (Eds.), *Governance without Government: Order and Change in World Politics* (Cambridge: Cambridge University Press, 1992).
- Rosenfeld, M., 'The Rule of Law and the Legitimacy of Constitutional Democracy', Cardozo Law School, Public Law Research Paper No. 36, (March 2001), available via: <http://ssrn.com/abstract=262350>, last accessed: 3 April 2017.
- Rossi, M., 'Europäisiertes internationales Umweltverwaltungsrecht', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 165-180.
- Ruffert, M., *Die Globalisierung als Herausforderung an das Öffentliche Recht* (Stuttgart: Boorberg, 2004).
- Ruffert, M., 'Perspektiven des Internationalen Verwaltungsrechts', in Möllers, C., Vosskuhle, A. & Walter, C. (Eds.), *Internationales Verwaltungsrecht – Eine Analyse Anhand von Referenzgebieten* (Tübingen: Mohr Siebeck, 2007), pp. 395-419.
- Ruffert, M., '§17 Rechtsquellen und Rechtsschichten des Verwaltungsrechts', in Hoffmann-Riem, W., Schmidt-Aßmann, E. & Voßkuhle, A. (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 1163-1255.
- Ruffert, M. & Steinecke, S., *The Global Administrative Law of Science* (Heidelberg/Dordrecht/London/New York: Springer, 2011).
- Ruffert, M. & Walter, C. (Eds.), *Institutionalisiertes Völkerrecht* (München: Verlag C.H. Beck, 2009).
- Sauer, F., 'Preface', in van de Laan, J. & DeGeorge, J. (Eds.), *Global Approach in Safety Testing – ICH Guidelines Explained* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. v-viii.
- Savino, M., 'EU "Procedural" Supranationalism: On Models for Global Administrative Law', available via: [http://www.law.nyu.edu/sites/default/files/-upload\\_documents/gffsavinopaper.pdf](http://www.law.nyu.edu/sites/default/files/-upload_documents/gffsavinopaper.pdf), last accessed: 3 April 2017.
- Savino, M. & De Bellis, M., 'An Unaccountable Trans-Governmental Branch? The Basle Committee', in Cassese, S., Carotti, B., Casini, L., Cavalieri, E. & MacDonald, E. (Eds.), *Global Administrative Law: The Casebook*, 3<sup>rd</sup> Edition, pp. 243-254, available via: <http://www.irpa.eu/wp-content/uploads/2012/08/The-Casebook-Chapter-1.pdf>, last accessed: 3 April 2017.
- Scott, C., 'Standard-Setting in Regulatory Regimes', in Baldwin, R., Cave, M. & Lodge, M. (Eds.), *The Oxford Handbook of Regulation* (Oxford: Oxford University Press, 2010), pp. 104-119.
- Scott, J., 'International Trade and Environmental Governance: Relating Rules (and Standards) in the EU and WTO', 15(2) *European Journal of International Law* (2004), pp. 307-354.
- Scott, J., 'In Legal Limbo: Post-Legislative Guidance as Challenge for Administrative Law', 48(2) *Common Market Law Review* (2011), pp. 329-355.
- Scott, J., 'The New EU "Extraterritoriality"', 51(5) *Common Market Law Review* (2014a), pp. 1343-1380.
- Scott, J., 'Extraterritoriality and Territorial Extension in EU Law', 62(1) *American Journal of Comparative Law* (2014b), pp. 87-125.
- Scott, J. & Sturm, S., 'Courts as Catalysts: Rethinking The Judicial Role in New Governance', 13(3) *The Columbia Journal of European Law* (2007), pp. 565-594.
- Scott, J. & Trubek, D., 'Mind the Gap: Law and New Approaches to Governance in the European Union', 8(1) *European Law Journal* (2003), pp. 1-18.
- Schachter, O., 'The Twilight Existence of Nonbinding International Agreements', 71(2) *The American Journal of International Law* (1977), pp. 296-304.

- Schäferhoff, M., Campe, S. & Kaan, C., 'Transnational Public-Private Partnerships in International Relations: Making Sense of Concepts, Research Frameworks, and Results', 11(3) *International Studies Review* (2009), pp. 451-474.
- Scharpf, F., *Demokratietheorie Zwischen Utopie und Anpassung* (Konstanz: Universitätsverlag Konstanz, 1970).
- Scharpf, F., *Governing in Europe – Effective and Democratic?* (Oxford: Oxford University Press, 1999).
- Schepel, H., *The Constitution of Private Governance – Product Standards in the Regulation of Integrating Markets* (Oxford: Hart, 2005).
- Schepel, H., 'The New Approach to the New Approach: The Juridification of Harmonized Standards in EU Law', 20(4) *Maastricht Journal of European and Comparative Law* (2013), pp. 521-533.
- Schmidt, V., 'Democracy and Legitimacy in the European Union Revisited: Input, Output and "Throughput"', 61(1) *Political Studies* (2013), pp. 2-22.
- Schmidt-Abmann, E., *Das allgemeine Verwaltungsrecht als Ordnungsidee – Grundlagen und Aufgaben der verwaltungsrechtlichen Systembildung*, 2<sup>nd</sup> Edition (Heidelberg: Springer, 2006).
- Schmidt-Abmann, E., 'The Internationalization of Administrative Relationships as a Challenge for Administrative Law Scholarship', in von Bogdandy, A., Wolfrum, R., von Bernstorff, J., Dann, P. & Goldmann, M. (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 943-963.
- Schneider, I., *Das Kooperationsprinzip im Vorfeld der Arzneimittelzulassung – Zum national und Europarechtlichen Rahmen des Zusammenwirken von Potentiellen Antragsstellern und Zulassungsbehörden* (Frankfurt am Main: Peter Lang Europäischer Verlag der Wissenschaften, 2003).
- Scholten, M., *The Political Accountability of EU and US Independent Regulatory Agencies* (Leiden: Brill Nijhoff, 2014).
- Schwarze, J., *EU Administrative Law* (London: Sweet and Maxwell, 2006).
- Schwarze, J., 'Soft Law im Recht der Europäischen Union', 1 *Europarecht* (2011), pp. 3-18.
- Senden, L., *Soft Law in European Community Law: Its Relationship to Legislation* (Nijmegen: Wolf Legal Publishers, 2003).
- Senden, L., 'Soft Post-Legislative Rulemaking: A Time for More Stringent Control?', 19(1) *European Law Journal* (2013), pp. 57-75.
- Shaffer, G. & Pollack, M., 'Hard and Soft Law', in Dunoff, J. & Pollack, M. (Eds.), *Interdisciplinary Perspectives on International Law and International Relations – The State of the Art* (Cambridge: Cambridge University Press, 2013), pp. 197-222.
- Shamir-Borer, E., 'Legitimacy without Authority in Global Standardization Governance: The Case of the International Organization for Standardization (ISO)', in Cassese, S., Carotti, B., Casini, L., Cavalieri, E. & MacDonald, E. (Eds.), *Global Administrative Law: The Casebook*, 3<sup>rd</sup> Edition, pp. 162-183, available via: <http://www.irpa.eu/wp-content/uploads/2012/08/The-Casebook-Chapter-1.pdf>, last accessed: 3 April 2017.
- Shapiro, M., 'Administrative Law Unbounded: Reflections on Government and Governance', 8(2) *Indiana Journal of Legal Studies* (2001), pp. 369-377.
- Shelton, D., 'Soft Law', in Armstrong, D. (Ed.), *Routledge Handbook of International Law* (Oxon: Routledge, 2009), pp. 68-80.
- Simonati, A., 'The Principles of Administrative Procedure and the EU Courts: An Evolution in Progress?', 4(1) *Review of European Administrative Law* (2011), pp. 45-81.
- Slaughter, A., 'The Real New World Order', 76(5) *Foreign Affairs* (1997), pp. 183-197.

- Slaughter, A., 'Agencies on the Loose? Holding Government Networks Accountable', in Bermann, G., Herdegen, M. & Lindseth, P. (Eds.), *Transatlantic Regulatory Cooperation: Legal Problems and Political Prospects* (Oxford: Oxford University Press, 2000), pp. 521-546.
- Slaughter, A., 'The Accountability of Government Networks', 8(2) *Indiana Journal of Global Legal Studies* (2001), pp. 347-367.
- Slaughter, A., *A New World Order* (Princeton/Oxford: Princeton University Press, 2004).
- Slaughter, A. & Zaring, D., 'Networking Goes International: An Update', 2 *Annual Review of Law and Social Science* (2006), pp. 211-229.
- Snyder, F., 'Soft Law and the Institutional Practice in the European Community', in Martin, S. (Ed.), *The Construction of Europe – Essays in Order of Emile Noel* (Dordrecht: Kluwer, 1994), pp. 197-225.
- Spina, A., 'The Regulation of Pharmaceuticals Beyond the State', in Chiti, E. & Mattarella, B. (Eds.), *Global Administrative Law and EU Administrative Law* (Heidelberg: Springer 2011), pp. 249-268.
- Ștefan, O. 'European Union Soft Law: New Developments Concerning the Divide Between Legally Binding Force and Legal Effects', 75(5) *The Modern Law Review* (2012), pp. 865-893.
- Ștefan, O., *Soft Law in Court: Competition Law, State Aid, and the Court of Justice of the European Union* (Alphen aan den Rijn: Kluwer, 2013).
- Ștefan, O., 'Helping Loose Ends Meet? The Judicial Acknowledgement of Soft Law as a Tool of Multi-Level Governance', 21(2) *Maastricht Journal of European and Comparative Law* (2014), pp. 359-378.
- Steffek, J., 'The Legitimation of International Governance', 9(2) *European Journal of International Relations* (2003), pp. 249-275.
- Steffek, J. & Ferretti, M., 'Accountability or "Good Decision"? The Competing Goals of Civil Society Participation in International Governance', 23(1) *Global Society* (2009), pp. 37-57.
- Stewart, R., 'The Reformation Of American Administrative Law', 88(8) *Harvard Law Review* (1975), pp. 1669-1813.
- Stewart, R., 'Administrative Law in the Twenty-First Century', 78(2) *New York University Law Review* (2003), pp. 437-460.
- Stewart, R., 'U.S. Administrative Law: A Model For Global Administrative Law?', 68(3&4) *Law and Contemporary Problems* (2005), pp. 63-108.
- Stigler, G., 'The Theory of Economic Regulation', 2(1) *The Bell Journal of Economics and Management Science* (1971), pp. 3-21.
- Tallberg, J., 'Delegation to Supranational Institutions: Why, How, and with What Consequence', 25(1) *West European Politics* (2002), pp. 23-46.
- Terpan, F., 'Soft Law in the European Union – The Changing Nature of EU Law', 21(1) *European Law Journal* (2015), pp. 68-96.
- Thürer, D., 'Soft Law', in Wolfrum, R. (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: Oxford University Press, 2016), Article last updated March 2009, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.
- Tietje, C., *Internationalisiertes Verwaltungsbandeln* (Berlin: Duncker & Humblot GmbH, 2001).
- Tietje, C., 'History of Transnational Administrative Networks', in Dilling, O., Herberg, M. & Winter, G. (Eds.), *Transnational Administrative Rule-Making – Performance, Legal Effects and Legitimacy* (Oxford/Portland: Hart Publishing, 2011), pp. 23-37.
- Timmermans, K., 'Harmonization, Regulation, and Trade: Interactions In The Pharmaceutical Field', 34(4) *International Journal of Health Services* (2004), pp. 651-661.

- Trubek, D., Cottrell, P. & Nance, M., ‘Soft law’, ‘Hard law’ and European Integration’, in de Búrca, G. & Scott, J. (Eds.), *Law and New Governance in the EU and the US* (Oxford/Portland: Hart Publishing, 2006), pp. 65-94.
- Trute, H.-H., ‘§6 Die demokratische Legitimation der Verwaltung’, in Hoffmann-Riem, W., Schmidt-Aßmann, E. & Voßkuhle, A. (Eds.), *Grundlagen des Verwaltungsrechts Band I* (München: Beck, 2012), pp. 341-435.
- Vaillancourt Rosenau, P. (Ed.), *Public-Private Policy Partnerships* (Cambridge, MA: MIT Press, 2000).
- Vamvakas, S., ‘EU Perspectives on ICH’, in van de Laan, J. & DeGeorge, J. (Eds.), *Global Approach in Safety Testing – ICH Guidelines Explained* (New York/Heidelberg/Dordrecht/London: Springer, 2013), pp. 13-22.
- van Asselt, M., Versluis, E. & Vos, E. (Eds.), *Balancing between Trade and Risk – Integrating Legal and Social Science Perspectives* (Oxon/New York: Routledge/Earthscan, 2013).
- van Asselt, M., Everson, M. & Vos, E., ‘The European Union Put to the Test: The Quest for Politics’, in Van Asselt, M., Everson, M. & Vos, E. (Eds.), *Trade, Health and the Environment – The European Union Put To The Test* (Oxon/New York: Routledge/Earthscan, 2014), pp. 9-21.
- van Gerstel, R. & Micklitz, H., ‘European Integration through Standardization : How Judicial Review is Breaking Down the Club House of Private Standardization Bodies’, 50(1) *Common Market Law Review* (2013), pp. 145-181.
- van Kersbergen, K. & van Waarden, F., ‘“Governance” as a Bridge between Disciplines: Cross-Disciplinary Inspiration Regarding Shifts in Governance and Problems of Governability, Accountability and Legitimacy’, 43(2) *European Journal of Political Research* (2004), pp. 143-171.
- van Rossem, J., ‘The EU at Crossroads: A Constitutional Inquiry into the way International Law is received within the EU Legal Order’, in Canizzaro, E., Palchetti, P. & Wessel, R. (Eds.), *International law as law of the European Union* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), pp. 59-89.
- van Vooren, B. & Wessel, R., ‘The EU as Global Legal Actor’, in van Vooren, B. & Wessel, R. (Eds.), *EU External Relations Law – Text, Cases and Materials* (Cambridge: Cambridge University Press, 2014), pp. 1-34.
- van Vooren, B., Blockmans, S. & Wouters, J. (Eds.), *The EU’s Role in Global Governance – The Legal Dimension* (Oxford: Oxford University Press, 2013).
- van Waarden, F., ‘Dimensions and Types of Policy Networks’, 21(1-2) *European Journal of Political Research* (1992), pp. 29-52.
- Vereinigung der Deutschen Staatsrechtslehrer, ‘Entterritorialisierung des Öffentlichen Rechts’, 76 *Veröffentlichungen der Vereinigung der Deutschen Staatsrechtslehrer* (2017).
- Vogel, D., ‘The Globalization of Pharmaceutical Regulation’, 11(1) *Governance* (1998), p. 1-22.
- Vogel, D., ‘The New Politics of Risk Regulation in Europe’, CARR Discussion Papers, DP 3, Centre for Analysis of Risk and Regulation, London School of Economics and Political Science, (2001).
- Vogel, D., *The Politics of Precaution- Regulating Health, Safety and Environmental Risks in Europe and the United States* (Princeton/Oxford: Princeton University Press, 2012).
- von Bogdandy, A., ‘General Principles of International Public Authority: Sketching a Research Field’, in von Bogdandy, A., Wolfrum, R., von Bernstorff, J., Dann, P. & Goldmann, M. (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 727-760.
- von Bogdandy, A., ‘The European Lesson for International Democracy – The Significance of Articles 9 to 12 EU Treaty for International Organizations’, 23(2) *European Journal of International Law* (2012), pp. 315-334.

- von Bogdandy, A., Dann, P. & Goldmann, M., 'Developing the Publicness of Public International Law', in von Bogdandy, A., Wolfrum, R., von Bernstorff, J., Dann, P. & Goldmann, M. (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010), pp. 3-32.
- von Bogdandy, A., Wolfrum, R., von Bernstorff, J., Dann, P. & Goldmann, M. (Eds.), *The Exercise of Public Authority by International Institutions: Advancing International Institutional Law* (Heidelberg: Springer, 2010).
- Vos, E., *Institutional Frameworks of Community Health and Safety Regulation – Committees, Agencies and Private Bodies* (Oxford: Hart Publishing, 1999).
- Vos, E., 'European Agencies and the Composite EU Executive', in Everson, M., Monda, C. & Vos, E. (Eds.), *European Agencies in Between Institutions and Member States* (Alphen aan den Rijn: Kluwer Law International, 2014), pp. 11-47.
- Vos, E., 'EU Agencies and Independence', in Ritleng, D. (Ed.), *Independence and Legitimacy in the Institutional System of the European Union* (Oxford: Oxford University Press, 2016), pp. 206-228.
- Vos, E. & Joerges, C., 'Structures of Transnational Governance and their Legitimacy', in Vervaele, J. (Ed.), *Compliance and Enforcement of European Union Law* (London: Kluwer, 1999), pp. 71-93, p. 90.
- Wallach, L., 'Accountable Governance in the Era of Globalization – The WTO, NAFTA and International Harmonization of Standards', 50(4) *Kansas Law Review* (2001-2002), pp. 823-865.
- Weber, M., *Wirtschaft und Gesellschaft – Grundriss der Verstehenden Soziologie, 5th Edition* (Tübingen: Mohr Siebeck, 1972).
- Weil, P., 'Towards relative normativity in international law?', 77(3) *American Journal of International Law* (1983), pp. 413-442.
- Weiler, J., 'The Geology of International Law – Governance, Democracy and Legitimacy', 64(3) *Zeitschrift für ausländisches öffentliches Recht und Völkerrecht* (2004), pp. 547-562.
- Weiler, J., Haltern, U. & Mayer, F., 'European Democracy and its Critique', 18(4) *West European Politics* (1995), pp. 4-39.
- Wessel, R., 'The Legal Framework for the Participation of the European Union in International Institutions', 33(6) *European Integration* (2011), pp. 621-635.
- Wessel, R., 'Reconsidering the Relationship between International and EU Law: Towards A Content-Based Approach?', in Canizzaro, E., Palchetti, P. & Wessel, R. (Eds.), *International Law as Law of the European Union* (Leiden/Boston: Martinus Nijhoff Publishers, 2012), pp. 7-33.
- Wheatley, S., 'Democratic Governance beyond the State: the Legitimacy of Non-State Actors as Standard-Setters', in Peters, A., Koechlin, L., Förster, T. & Fenner Zinkernagel, G. (Eds.), *Non-State Actors as Standard-Setters* (Cambridge: Cambridge University Press, 2009), pp. 215-240.
- White, N., *The Law of International Organisations*, 2<sup>nd</sup> Edition, (Manchester: Manchester University Press, 2005).
- Wiener, J., 'The Rhetoric of Precaution', in Wiener, J., Rogers, M., Hammitt, J. & Sand, P. (Eds.), *The Reality of Precaution: Comparing Risk Regulation in the United States and Europe* (London: Routledge, 2011), pp. 3-39.
- Wolfrum, R., 'Legitimacy in International Law', in Wolfrum, R. (Ed.), *The Max Planck Encyclopedia of Public International Law* (Oxford: University Press Oxford, 2016), Article last updated March 2011, available via: [opil.ouplaw.com/home/EPIL](http://opil.ouplaw.com/home/EPIL), last accessed: 3 April 2017.
- Wouters, J. & Verhoeven, S., 'Regulation and Globalization: Interaction between International Standard-Setting Agencies and the European Union', in Geradin, D.,

- Muñoz, R. & Petit, N. (Eds.), *Regulation Through Agencies in the EU: A New Paradigm of European Governance* (Cheltenham: Edward Elgar, 2006), pp. 246-273.
- Wouters, J., Odermatt, J. & Ramopoulos, T., 'The EU in the World of International Organizations: Diplomatic Aspirations, Legal Hurdles and Political Realities', Leuven Centre for Global Governance Studies, Working Paper 121, (September 2013).
- Zaring, D., 'Informal Procedure, Hard and Soft, in International Administration', 5(2) *Chicago Journal of International Law* (2005), pp. 547-603.
- Zürn, M., 'Global Governance and Legitimacy Problems', 39(2) *Government and Opposition* (2004), pp. 260-287.
- Zurek, K., *European Food Regulation after Enlargement: Facing the Challenges of Diversity* (Leiden/Boston: Martinus Nijhoff Publishers, 2012).

## EU LAW

- Single European Act, OJ L 169, 29 June 1987, pp. 1-29.
- Consolidated version of the Treaty on the European Union, OJ C 326, 26 October 2012, pp. 13-46.
- Consolidated version of the Treaty on the Functioning of the European Union, OJ C 326, 26 October 2012, pp. 47-390.
- Charter of Fundamental Rights of the European Union, OJ C 326, 26 October 2012, pp. 391-407.
- Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, OJ L 18, 22 January 2000, pp. 1-5.
- Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31 May 2001, pp. 43-48.
- Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority, and laying down procedures in matters of food safety, OJ L 31, 1 February 2002, pp. 1-24.
- Regulation (EC) No 2099/2002 of the European Parliament and of the Council of 5 November 2002 establishing a Committee on Safe Seas and the Prevention of Pollution from Ships (COSS) and amending the Regulations on maritime safety and prevention of pollution from ships, OJ L 324, 29 November 2002, pp. 1-5.
- Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use, and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 136, 30 April 2004, pp. 1-33.
- Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ L 378, 27 December 2006, pp. 1-19.
- Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93, and Commission Regulation (EC) No 1488/94, as well as Council Directive 76/769/EEC, and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC, OJ L 396, 30 December 2006, pp. 1-849.

- Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004, OJ L 324, 10 December 2007, pp. 121-137.
- Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 348, 31 December 2010, pp. 1-16.
- Regulation (EU) No 182/2011 of the European Parliament and of the Council of 16 February 2011 laying down the rules and general principles concerning mechanisms for control by Member States of the Commission's exercise of implementing powers, OJ L 55, 28 February 2011, pp. 13-18.
- Regulation (EU) No 1025/2012 of the European Parliament and of the Council of 25 October 2012 on European standardization, OJ L 316, 25 October 2012, pp. 12-33.
- Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, OJ L 158, 27 May 2014, pp. 1-76.
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use, OJ L 121, 1 May 2001, pp. 34-44.
- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, OJ L 311, 28 November 2001, pp. 67-128.
- Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 136, 30 April 2004, pp. 85-90.
- Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 136, 30 April 2004, pp. 34-57.
- Directive 2004/36/EC of the European Parliament and of the Council of 21 April 2004 on the safety of third-country aircraft using Community airports, OJ L 143, 30 April 2004, pp. 76-86.
- Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products, OJ L 91, 9 April 2005, pp. 13-19.
- Directive 2006/23/EC of the European Parliament and of the Council of 5 April 2006 on a Community air traffic controller license, OJ L 114, 27 April 2006, pp. 22-37.
- Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use Text with EEA relevance, OJ L 348, 31 December 2010, pp. 74-99.
- Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products, OJ L 174, 1 July 2011, pp. 74-87.

- Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products, OJ L 214, 24 August 1993, pp. 1-21.
- Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ 22, 9 February 1965, pp. 369-373.
- Council Directive 75/318/EEC of 20 May 1975 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of proprietary medicinal products, OJ L 147, 9 June 1975, pp. 1-12.
- Second Council Directive 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ L 147, 9 June 1975, pp. 13-22.
- Council Directive 83/570/EEC of 26 October 1983 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ L 332, 28 November 1983, pp. 1-10.
- Council Directive 87/22/EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology, OJ L 15, 17 January 1987, pp. 38-41.
- Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems, OJ L 40, 11 February 1989, pp. 8-11.
- Council Directive 89/341/EEC of 3 May 1989 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products, OJ L 142, 25 May 1989, pp. 11-13.
- Council Directive 89/342/EEC of 3 May 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for immunological medicinal products consisting of vaccines, toxins or serums and allergens, OJ L 142, 25 May 1989, pp. 14-15.
- Council Directive 89/343/EEC of 3 May 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for radiopharmaceuticals, OJ L 142, 25 May 1989, pp. 16-18.
- Council Directive 89/381/EEC of 14 June 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products and laying down special provisions for medicinal products derived from human blood or human plasma, OJ L 181, 28 June 1989, pp. 44-46.
- Council Directive 92/27/EEC of 31 March 1992 on the labelling of medicinal products for human use and on package leaflets, OJ L 113, 30 April 1992, pp. 8-12.
- Council Directive 92/28/EEC of 31 March 1992 on the advertising of medicinal products for human use, OJ L 113, 30 April 1992, pp. 13-18.
- Council Directive 92/73/EEC of 22 September 1992 widening the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to medicinal products and laying down additional provisions on homeopathic medicinal products, OJ L 297, 13 October 1992, pp. 8-11.

- Council Directive 93/39/EEC of 14 June 1993 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC in respect of medicinal products, OJ L 214, 24 August 1993, pp. 22-30.
- Council Decision 75/320/EEC of 20 May 1975 setting up a pharmaceutical committee, OJ L 147, p. 23.
- Council Decision 1999/468/EC laying down the procedures for the exercise of implementing powers conferred on the Commission, OJ L184, 17 July 1999, pp. 23-26
- Council Decision 2003/822/EC of 17 November 2003 on the accession of the European Community to the Codex Alimentarius Commission, OJ L 209, 17 November 2003, pp. 14-21.
- Council Recommendation 83/571/EEC of 26 October 1983 concerning tests relating to the placing on the market of proprietary medicinal products, OJ L332, 28 November 1983, pp. 11-32.
- Commission Directive 2003/63/EC of 25 June 2003 amending Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use, OJ L 159, 25 June 2003, pp. 46-94.
- Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use, OJ L 262, 14 October 2003, pp. 22–26.
- Commission Decision C(2015) 7256 final of 23 October 2015 on the participation of the Commission as Founding Regulatory Member in the ‘International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use’. This decision is not in the public domain but has been obtained through an access to documents request. A copy is on file with the author.
- Commission Implementing Decision C(2012) 3306 final of 25 May 2012 refusing a marketing authorisation under Regulation (EC) No 726/2004 of the European Parliament and of the Council for “Orphacol – Cholic acid”, an orphan medicinal product for human use.
- Commission Implementing Decision C(2013) 5934 final, granting, in exceptional circumstances, marketing authorisation under Regulation No 726/2004 for ‘Orphacol (Cholic Acid)’, an orphan medicinal product for human use.
- Commission Delegated Regulation (EU) No 1252/2014 of 28 May 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council with regard to principles and guidelines of good manufacturing practice for active substances for medicinal products for human use, OJ L 337, 25 November 2014, pp. 1-7.

## EU CASE LAW

- Case 9/56 *Meroni and Co., Industrie Metallurgiche S.p.A. v. Highby Authority*, ECLI:EU:C:1958:7.
- Case 10/56 *Meroni and Co., Industrie Metallurgiche S.p.A. v. Highby Authority*, ECLI:EU:C:1958:8.
- Case C-25/62 *Plaumann & Co. v. Commission of the European Economic Community*, ECLI:EU:C:1963:17.
- Case 22/70 *Commission v. Council (ERTA)*, ECLI:EU:C:1971:32.
- Joined cases 21 to 24/72 *International Fruit Company v. Produktschap voor Groenten en Fruit*, ECLI:EU:C:1972:115.
- Case 181/73 *Haegeman v. Belgium*, ECLI:EU:C:1974:41
- Opinion 1/76 of the Court of 26 April 1977, Opinion given pursuant to Article 228 (1) of the EEC Treaty – ‘Draft Agreement establishing a European Laying-up Fund for Inland Waterway Vessels’, ECLI:EU:C:1977:63.

- Case 60/81 *IBM v. Commission*, ECLI:EU:C:1981:264.
- Case 104/81 *Hauptzollamt Mainz v. Kupferberg*, ECLI:EU:C:1982:362.
- Case C-227/82 *Criminal proceeding against Leendert van Bennekom*, ECLI:EU:C:1983:354.
- Case 294/83 *Les Verts v. Parliament*, ECLI:EU:C:1986:166.
- Case C-35/85 *Procureure de la Republique v. Gerard Tissier*, ECLI:EU:C:1986:143.
- Case 178/84 *Commission v. Germany*, ECLI:EU:C:1987:126.
- Case C-12/86 *Demirel*, ECLI:EU:C:1987:400.
- Case 70/87 *Fediol v. Commission*, ECLI:EU:C:1989:254.
- Case 30/88 *Greece v. Commission*, EU:C:1989:422.
- Case C-322/88 *Salvatore Grimaldi v. Fonds des Maladies Professionnelles*, ECLI:EU:C:1989:646.
- Case C-366/88 *France v. Commission (Internal instructions)*, ECLI:EU:C:1990:348.
- Case C-369/88 *Criminal proceedings against Jean-Marie Delattre*, ECLI:EU:C:1991:137.
- Case C-69/89 *Nakajima v. Council*, ECLI:EU:C:1991:186.
- Case C-313/90 *Comité International de la Rayonne et des Fibres Synthétique (CIRFS) and Others v. Commission*, ECLI:EU:C:1993:111.
- Case C-188/91 *Deutsche Shell v. Hauptzollamt Harburg-Harburg*, ECLI:EU:C:1993:24.
- Case C-325/91 *France v. Commission*, ECLI:EU:C:1993:245.
- Case C-327/91 *French Republic v. Commission*, ECLI:EU:C:1994:305.
- Case T-3/93 *Air France v. Commission*, ECLI:EU:T:1994:36.
- Case C-280/93 *Germany v. Council*, ECLI:EU:C:1994:367.
- Case C-61/94 *Commission v. Germany*, ECLI:EU:C:1996:313.
- Case C-311/94 *IJssel-Vliet Combinatie v. Minister van Economische Zaken*, ECLI:EU:C:1996:383.
- Case C-57/95 *France v. Commission*, ECLI:EU:C:1997:164.
- Case T-214/95 *Vlaamse Gewest v. Commission*, ECLI:EU:T:1998:77.
- Case C-149/96 *Portugal v. Council*, ECLI:EU:C:1999:574.
- Case C-443/97 *Spain v. Commission*, ECLI:EU:C:2000:190.
- Case T-13/99 *Pfizer Animal Health v. Council*, ECLI:EU:T:2002:209.
- Case T-326/99 *Nancy Fern Olivieri v. Commission*, ECLI:EU:T:2003:351.
- Case C-382/99 *Netherlands v. Commission*, ECLI:EU:C:2002:363.
- Case C-50/00P *Unión de Pequeños Agricultores (UPA) v. Council of the European Union*, ECLI:EU:C:2002:462.
- Joined cases T-74/00, T-76/00, T-83/00, T-84/00, T-85/00, T-132/00, T-137/00 and T-141/00 *Artegodan GmbH and Others v. Commission of the European Communities*, ECLI:EU:T:2002:283.
- C-236/01 *Monsanto Agricoltura Italia SpA and Others and Presidenza del Consiglio dei Ministri and others*, ECLI:EU:C:2003:431.
- Case C-106/01 *Novartis Pharmaceuticals UK Ltd v. The Licensing Authority established by the Medicines Act 1968*, ECLI:EU:C:2004:245.
- Case C-286/02 *Bellio F.lli*, ECLI:EU:C:2004:212.
- Case C-233/02 *French Republic v. Commission*, ECLI:EU:C:2004:173.
- Joined cases C-189, 202, 205, 208 and 213/02 P *Dansk Rørindustri and others v. Commission*, ECLI:EU:C:2005:408.
- Case C-377/02 *Van Parys v. Belgische Interventie- en Restitutiebureau*, ECLI:EU:C:2005:121.
- Case 196/05 *Sachsenmilch v. Oberfinanzdirektion Nürnberg*, ECLI:EU:C:2006:383.
- Joined cases C-154/04 and C-155/04 *Alliance for Natural Health*, ECLI:EU:C:2005:449.
- Case C-344/04 *International Air Transport Association and Others (IATA)*, ECLI:EU:C:2006:10.
- Case T-374/04 *Germany v. Commission*, ECLI:EU:T:2007:332.
- Case T-133/03 *Schering-Plough Ltd. v. Commission and EMEA*, ECLI:EU:T:2007:365.
- C-319/05 *Commission v. Germany*, ECLI:EU:C:2007:678.

- Joined cases C-39/05P and C-52/05P *Kingdom of Sweden and Maurizio Turco v. Council*, ECLI:EU:C:2008:374.
- Case T-73/04 *Carbone-Lorraine v. Commission*, ECLI:EU:T:2008:416.
- Joined cases C-402 and 415/05P *Kadi & Al Barakaat International Foundation v. Council & Commission*, ECLI:EU:C:2008:461.
- Case T-411/06 *Sogelma v. EAR*, ECLI:EU:T:2008:419.
- Case C-140/07 *Hecht-Pharma GmbH v. Staatliches Gewerbeaufsichtsamt Lüneburg*, ECLI:EU:C:2009:5.
- Case T- 52/09 *Nycomed Danmark v. EMA*, ECLI:EU:C:2011:83.
- Case T-18/10 *Inuit Tapiriit Kanatami and Others v. Parliament and Council*, ECLI:EU:T:2011:419.
- Case T-262/10 *Microban International Ltd and Microban (Europe) Ltd v. European Commission*, ECLI:EU:T:2011:623.
- Case T-539/10 *Acino AG v. Commission*, ECLI:EU:T:2013:110.
- C-171/11 *Fra.bo SpA v. Deutsche Vereinigung de Gas- und Wasserfaches eV (DGVW) – Technisch Wissenschaftlicher Verein*, ECLI:EU:C:2012:45.
- Case C-308/11 *Chemische Fabrik Kreussler v. Sunstar Deutschland*, ECLI:EU:C:2012:548.
- Case C-583/11 *Inuit Tapiriit Kanatami and Others v. Parliament and Council*, ECLI:EU:C:2013:625.
- Case T-301/12 *Laboratoires CTRS v. European Commission*, ECLI:EU:C:2014:214
- Case C-99/12 *Federal Republic of Germany v. Council of the European Union*, ECLI:EU:C:2014:2258.
- Case T-44/13 R *Order of the President of the General Court of 25 April 2013 in AbbVie v. EMA*, ECLI:EU:T:2013:221.
- Case T-73/13 R *Order of the President of the General Court of 25 April 2013 in InterMune UK and Others v. EMA*, ECLI:EU:T:2013:222.
- Case C-269/13P *Acino AG v. Commission*, ECLI:EU:C:2014:255.
- Case C-615/13P *ClientEarth and Pesticide Action Network Europe (PAN Europe) v. European Food Safety Authority*, ECLI:EU:C:2015:489.
- Case C-660/13 *Council v. Commission*, ECLI:EU:C:2016:616.

#### OTHER EU DOCUMENTS

- Council of the European Union – General Secretariat, Notice of Meeting and Provisional Agenda – Working Party on Pharmaceuticals and Medical Devices Friday 19 July 2013, CM 3637/13, available via: <http://data.consilium.europa.eu/doc/document/CM-3637-2013-INIT/en/pdf>, last accessed: 3 April 2017.
- ECHA, Multi-Annual Work Programme 2014-2018, ECHA-13-A-06.01-EN, September 2013.
- European Commission, Notice on exclusive dealing constructs with commercial agents (OJ 139, 24 December 1962, p. 2921).
- European Commission, Notice on patent licensing agreements (OJ 139, 24 December 1962, p. 2922).
- European Commission, White Paper from the Commission to the European Council – Completing the Internal Market, COM(85) 310 final, Brussels, 14 June 1985.
- European Commission, Report from the Commission to the Council on the Activities of the Committee for Proprietary Medicinal Products, COM(91) 39 final, Brussels, 15 February 1991.
- European Commission, European Governance – A White Paper, COM(2001) 428 final, OJ 287, 12 October 2001, pp. 1-29.

- European Commission, Report from the Commission on the experience acquired as a result of the operation of the procedures for granting marketing authorisations for medicinal products laid down in Regulation (EEC) No 2309/93, in chapter III of Directive 75/319/EEC and chapter IV of Directive 81/851/EEC, COM(2001) 606 final, Brussels, 23 October 2001.
- European Commission, Towards a reinforced culture of consultation and dialogue – General principles and minimum standards for consultation of interested parties by the Commission, COM(2002) 704 final, Brussels, 11 December 2002.
- European Commission, Green Paper on Public-Private Partnerships and Community Law on Public Contracts and Concessions, COM(2004) 374 final.
- European Commission, Notice to Applicants, Volume 2A Procedures for marketing authorisation, Chapter 4 Centralised Procedure, Brussels, April 2006, ENTR/F2/BLD(2006), available via: [http://ec.europa.eu/health/documents/eudralex/vol-2/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-2/index_en.htm), last accessed: 3 April 2017.
- European Commission, Guideline on the definition of a potential serious risk to public health in the context of Article 29(1) and (2) of Directive 2001/83/EC, OJ C 133, 8 June 2006, pp. 5-7.
- European Commission, ‘Global Europe: competing in the world’, COM(2006) 567, 4 October 2006.
- European Commission, Guidance on a new Therapeutic Indication for a Well Established Substance., Brussels, November 2007.
- European Commission, Volume 2B – Notice to Applicants – Medicinal Products for Human Use, (Update May 2008), p. 2, available via: [http://ec.europa.eu/-health/files/eudralex/vol-2/b/update\\_200805/ctd\\_05-2008\\_en.pdf](http://ec.europa.eu/-health/files/eudralex/vol-2/b/update_200805/ctd_05-2008_en.pdf), last accessed: 3 April 2017.
- European Commission, Commission Communication – Guideline on the format and content of applications of agreement or modification of a paediatric investigation plan and request for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies (OJ C 243, 24 September 2008), pp. 1-12.
- European Commission, Communication from the Commission to the Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector, COM(2008) 666 final, Brussels, 10 December 2008.
- European Commission, Impact Assessment Guidelines, SEC(2009) 92, Brussels, 15 January 2009.
- European Commission, Guideline on the readability of the labelling and package leaflet of medicinal products for human use, ENTR/F/2/SF/jr (2009)D/869, 12 January 2009.
- European Commission, DG Competition, Pharmaceutical Sector Inquiry –Final Report, Adopted 9 July 2009, available via: [http://ec.europa.eu/competition/-sectors/pharmaceuticals/inquiry/staff\\_working\\_paper\\_part1.pdf](http://ec.europa.eu/competition/-sectors/pharmaceuticals/inquiry/staff_working_paper_part1.pdf), last accessed: 3 April 2017.
- European Commission, Press Release – Barroso unveils his new team, Brussels 27 November 2009, available via [http://europa.eu/rapid/press-release\\_IP-09-1837\\_en.htm?locale=en](http://europa.eu/rapid/press-release_IP-09-1837_en.htm?locale=en), last accessed: 3 April 2017.
- European Commission, Communication from the Commission — Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1), (2010/C 82/01).

- European Commission, 'Trade, Growth and World Affairs – Trade Policy as a Core Component Of the EU's 2020 Strategy', COM(2010) 612, 9 November 2010.
- European Commission, Communication from the Commission — Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3'), (2011/C 172/01).
- European Commission, Vademecum on the External Action of the European Union, SEC(2011)881/3.
- European Commission, Eudrallex – The Rules Governing Medicinal Products in the European Union – Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use – Introduction, SANCO/C8/AM/sl/ares(2010)1064597, available via: [https://ec.europa.eu/health/documents/eudrallex/vol-4\\_en](https://ec.europa.eu/health/documents/eudrallex/vol-4_en), last accessed: 3 April 2017.
- European Commission, Eudrallex – The Rules Governing Medicinal Products in the European Union – Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use – Chapter 1 Pharmaceutical Quality System, SANCO/AM/sl/ddg1.d.6(2012)860362, available via: [https://ec.europa.eu/health/documents/eudrallex/vol-4\\_en](https://ec.europa.eu/health/documents/eudrallex/vol-4_en), last accessed: 3 April 2017.
- European Commission, 70th meeting of the Pharmaceutical Committee, 27 March 2013, PHARM 621, International developments – Agenda Item 5a) Information from the Commission on the Reform of the ICH and the Regulators Forum, available via: <https://ec.europa.eu/health/sites/health/files/files/committee/-70meeting/pharm621.pdf>, last accessed: 3 April 2017.
- European Commission, 74th meeting of the Pharmaceutical Committee, 17 March 2015, PHARM 686, Agenda Item 4a International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), Presentation of the European Commission 'ICH Reform State-of-play and next steps', 17 March 2015, available via: <http://ec.europa.eu/health/files/committee/74meeting/pharm686.pdf>, last accessed: 3 April 2017.
- European Commission, Guideline on the Packaging Information of Medicinal Products for Human Use Authorised by the Union, July 2015, Revision 14.3, available via: [http://ec.europa.eu/health/files/eudrallex/vol-2/2015-07\\_14\\_3\\_packaging.pdf](http://ec.europa.eu/health/files/eudrallex/vol-2/2015-07_14_3_packaging.pdf), last accessed: 3 April 2017.
- European Commission, 75th meeting of the Pharmaceutical Committee, 21 October 2015, PHARM 701, Summary Record, available via: [https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pharm701\\_summary\\_record.pdf](https://ec.europa.eu/health/sites/health/files/files/committee/75meeting/pharm701_summary_record.pdf), last accessed: 3 April 2017.
- European Commission, Lenita Lindström-Gommers, Presentation at the 76th Pharmaceutical Committee, 28 April 2016, via: [http://ec.europa.eu/health/files/committee/76meeting/pharm710\\_5ai\\_ich\\_reform\\_presentation.pdf](http://ec.europa.eu/health/files/committee/76meeting/pharm710_5ai_ich_reform_presentation.pdf), last accessed: 3 April 2017.
- European Commission, 2013 Annual Activity Report Directorate General for Health and Consumers, available via: [https://ec.europa.eu/info/publications/annual-activity-report-2013-health-and-consumers\\_en](https://ec.europa.eu/info/publications/annual-activity-report-2013-health-and-consumers_en), last accessed: 3 April 2017.
- European Commission, 2014 Annual Activity Report Directorate General for Health and Consumers, available via: [https://ec.europa.eu/info/publications/annual-activity-report-2014-health-and-consumers\\_en](https://ec.europa.eu/info/publications/annual-activity-report-2014-health-and-consumers_en), last accessed: 3 April 2017.
- European Commission, 2015 Annual Activity Report Directorate General for Health and Food Safety, Ref. Ares(2016)1611103 – 05/04/2016, p. 9, available via: [https://ec.europa.eu/info/sites/info/files/activity-report-2015-dg-sante\\_april2016\\_en.pdf](https://ec.europa.eu/info/sites/info/files/activity-report-2015-dg-sante_april2016_en.pdf), last accessed: 3 April 2017.

- European Court of Auditors, Management of Conflict of Interest in selected EU Agencies, Special Report 15/2012.
- EEA Joint Committee, Decision of the EEA Joint Committee N74/1999 of 28 May 1999 amending Protocol 37 and Annex II (technical regulations, standards, testing and certification) to the EEA Agreement, OJ L 284, 9 November 2000, pp. 65-70.
- EMA, CPMP Note for Guidance on clinical investigation of drugs used in weight control (CPMP/EWP/281/96).
- EMA, CPMP Note for guidance on carcinogenic potential, CPMP/SWP/2877/00.
- EMA, Note for Guidance on Good Manufacturing Practice for Active Pharmaceutical Ingredients, November 2000, CPMP/ICH/4106/00.
- EMA, Note for guidance on minimising the risk of transmitting animal spongiform encephalopathogens via human and veterinary medicinal products (EMEA/410/01 Rev. 2 – October 2003) adopted by the Committee for Proprietary Medicinal Products (CPMP) and by the Committee for Veterinary Medicinal products (CVMP).
- EMA, Overview of comments received on draft guideline procedure for EU guidelines and related documents within the pharmaceutical legislative framework, EMEA/125817/2004, 24 June 2005, p. 3.
- EMA, Committee for Medicinal Products for Human Use, Rules of Procedure, EMEA/45110/2007.
- EMA, Status of EMEA Scientific Guidelines and European Pharmacopoeia Monographs and chapters in the regulatory framework applicable to medicinal products, 11 September 2008, EMEA/42371/2008 – corr.
- EMA, CHMP, Guideline on medicinal products for the treatment of insomnia, EMA/CHMP/16274/2009.
- EMA, Procedure For European Union Guidelines And Related Documents Within The Pharmaceutical Legislative Framework, EMEA/P/24143/2004 Rev. 1 corr., 18 March 2009.
- EMA, Press Release – European Medicines Agency recommends withdrawal of benfluorex from the market in the European Union, EMA/CHMP/815033/2009, 18 December 2009, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Press\\_release/2010/01/WC500059714.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/01/WC500059714.pdf), last accessed: 3 April 2017.
- EMA, Press Release – European Medicines Agency recommends suspension of Avandia, Avandamet and Avaglim, EMA/585784/2010, 23 September 2010, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/-Press\\_release/2010/09/WC500096996.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/-Press_release/2010/09/WC500096996.pdf), last accessed: 3 April 2017.
- EMA, Road map to 2015 – The European Medicines Agency’s contribution to science, medicines and health, Adopted by the Agency’s Management Board on 16 December 2010.
- EMA, Framework for interaction between the European Medicines Agency and health care professionals, EMA/688885/2010, 15 December 2011.
- EMA, Decision on rules relating to Articles 11a and 13 of the Staff Regulations concerning the handling of declared interests of employees of the European Medicines Agency, 1 February 2012, EMA/MB/500408/2011.
- EMA, Standard operating procedure: Arrangements for handling of conflicts of interest for EMA scientific meetings, SOP/EMA/0126, 8 October 2012.
- EMA, Best expertise vs conflict of interests: Striking the right balance, Report from the public workshop hosted by the European Medicines Agency in London on 6 September 2013, EMA/548247/2013.

- EMA, Assessment Report Orphacol, EMA/596651/2013, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Public\\_assessment\\_report/human/001250/WC500131542.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/001250/WC500131542.pdf), last accessed: 3 April 2017.
- EMA, Work Programme 2014, 12 December 2013, EMA/695772/2013.
- EMA, The European regulatory system for medicines and the European Medicines Agency – A consistent approach to medicines regulation across the European Union, (2014), EMA/437313/2014.
- EMA, Reflection paper on the requirements for selection and justification of starting materials for manufacture of chemical active substances, EMA/448443/2014, 16 September 2014.
- EMA, Explanatory Note on the fees payable to the European Medicines Agency, EMA/800328/2013, 20 March 2014.
- EMA, Guidance for applicants seeking scientific advice and protocol assistance, EMA/691788/2010 Rev. 7, 19 September 2014.
- EMA, Revised framework for interaction between the European Medicines Agency and patients and consumers and their organisations, EMA/637573/2014, 16 October 2014, p. 3.
- EMA, Work Programme 2015, 18 December 2014, EMA/773839/2014 Rev. 1.
- EMA, Framework for interaction between the European Medicines Agency and industry stakeholders, EMA/591272/2014, 2 October 2015.
- EMA, The European Medicines Agency Code of Conduct, EMA/385894/2012 rev.1, 16 June 2016.
- EMA, Work Programme 2016, 5 July 2016, EMA/92499/2016 Rev. 1.
- EMA, 2015 Annual report on independence, EMA/175527/2016, 16 September 2016.
- EMA, European Medicines Agency policy on the handling of declarations of interests of scientific committee’s members and experts, EMA/626261/2014 Rev.1, 6 October 2016.
- EMA, Decision on rules relating to Articles 11, 11a and 13 of the Staff Regulations concerning the handling of declared interests of staff members of the European Medicines Agency and candidates before recruitment, EMA/259494/2016, 6 October 2016.
- EMA, Overview of comments received by EMA on ‘ICH guideline E17 on general principles for planning and design of multi-regional clinical trials – Step 2b’, EMA/CHMP/ICH/453276/2016, 10 February 2017, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Overview\\_of\\_comments/2017/02/WC500221551.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2017/02/WC500221551.pdf), last accessed: 3 April 2017.
- EMA, Overview of comments received by EMA on ‘Questions and answers – ICH S9 guidelines on nonclinical evaluation for anticancer pharmaceuticals – Setp 2b’, EMA/CHMP/ICH/454684/2016, 10 February 2017, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Overview\\_of\\_comments/2017/02/WC500221552.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2017/02/WC500221552.pdf), last accessed: 3 April 2017.
- EMA, Overview of comments received by EMA on ‘ICH guideline Q11 on development and manufacture of drug substances (chemical entities and biotechnological/biological entities – questions and answers, EMA/CHMP/809509/2016, 21 March 2017, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Overview\\_of\\_comments/2017/03/WC500224269.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Overview_of_comments/2017/03/WC500224269.pdf), last accessed: 3 April 2017.
- EMA, Working with healthcare professionals, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Leaflet/2013/03/WC500140714.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2013/03/WC500140714.pdf), last accessed: 3 April 2017.

- EMA, Annual Report 2014, available via: [http://www.ema.europa.eu/docs/-en\\_GB/document\\_library/Annual\\_report/2015/04/WC500186306.pdf](http://www.ema.europa.eu/docs/-en_GB/document_library/Annual_report/2015/04/WC500186306.pdf), last accessed: 3 April 2017.
- EMA, Annual Report 2015, available via: [http://www.ema.europa.eu/docs/-en\\_GB/document\\_library/Annual\\_report/2016/05/WC500206482.pdf](http://www.ema.europa.eu/docs/-en_GB/document_library/Annual_report/2016/05/WC500206482.pdf), last accessed: 3 April 2017.
- EMA, Annexes to the annual report of the European Medicines Agency 2015, p. 57f, available via: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/-Annual\\_report/2016/05/WC500206481.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/-Annual_report/2016/05/WC500206481.pdf), last accessed: 3 April 2017.
- European Ombudsman, The European Code of Good Administrative Behaviour, available via: <http://www.ombudsman.europa.eu/en/resources/code.faces#/page/1>, last accessed: 3 April 2017.
- European Ombudsman, Ombudsman applauds European Medicines Agency's new transparency policy, Press Release no. 22/210, 01 December 2010, available via: <http://www.ombudsman.europa.eu/en/press/release.faces/en/5498/html.bookmark>, last accessed: 3 April 2017.
- European Ombudsman, Decision of the European Ombudsman closing her inquiry into complaint 1877/2010/FOR against the European Medicines Agency, 2 December 2013.
- European Ombudsman, Decision on own-initiative inquiry OI/3/2014/FOR concerning the partial refusal of the European Medicines Agency to give public access to studies related to the approval of a medicinal product, 8 June 2016.
- European Ombudsman, Decision on own-initiative inquiry OI/3/2014/FOR concerning the partial refusal of the European Medicines Agency to give public access to studies related to the approval of a medicinal product, Press release no. 6/2016, 10 June 2016.
- European Parliament, Resolution A5-0245/2001 on the European Ombudsman's Special Report to the European Parliament following the own-initiative inquiry into the existence and the public accessibility, in the different Community institutions and bodies, of a Code of Good Administrative Behaviour (C5-0438/2000 – 2000/2212 (COS)), 6 September 2001.
- European Parliament, Parliamentary Question (E-0561/06), 15 February 2006.
- European Parliament – Committee on Legal Affairs, Working Document on institutional and legal implications of the use of “soft law” instruments, Rapporteur: Manuel Medina Ortega, 14 February 2007, PE 384.581v02-00, p. 2.
- European Parliament and European Commission, Framework Agreement on relations between the European Parliament and the European Commission, OJ L 204/47, 20 November 2010.
- European Parliament, Decision of 25 October 2011 on discharge in respect of the implementation of the budget of the European Medicines Agency for the financial year 2009 (C7-0233/2010 – 2010/2173(DEC)).
- European Parliament – Directorate General for Internal Policies, Checks and Balances of Soft EU Rule-Making, Study by L. Senden & A. van den Brink, March 2012, PE 462.433.
- European Parliament, Decision of 10 May 2012 in Discharge in Respect of the Implementation of the Budget of the European Medicines Agency for the Financial Year 2010, (C7-0281/2011 – 2011/2220 (DEC)).
- European Parliament, Council of the European Union and European Commission, ‘Joint Statement of the European Parliament, Council of the EU and European Commission on decentralised agencies’, 19 July 2012.
- European Parliament, Resolution of 15 January 2013 with recommendations to the Commission on a Law of Administrative Procedure of the European Union (2012/2024(INL)), P7\_TA(2013)0004.

- European Parliament, Parliamentary Question (E-004699-13), 26 April 2013.
- European Parliament, Rules of Procedure, 8th Parliamentary term, July 2014.
- European Parliament, Committee on the Environment, Public Health and Food Safety, Draft Agenda Meeting 12 and 13 October 2015, ENVI(2015)1012\_1.
- European Parliament, Resolution of 28 April 2016 with observations forming an integral part of the decision on discharge in respect of the implementation of the budget of the European Medicines Agency for the financial year 2014, (2015/2171(DEC)).
- European Parliament, A regulation for an open, efficient and independent European Union administration, Resolution of 9 June 2016, 2016/2610 RSP, P8\_TA(2016)0279.
- European Parliament, Committee on the Environment, Public Health and Food Safety, Draft Agenda Meeting 7 and 8 November 2016, ENVI(2016)1107\_1.

#### INTERNATIONAL LAW

- Statute of the International Court of Justice, 18 April 1946.
- OECD, Convention on the Organisation for Economic Co-operation and Development of 14 December 1960.
- WHO, Constitution of the World Health Organisation, 22 July 1946.
- WHO/FAO, Statutes of the Codex Alimentarius Commission (Adopted in 1961 by the 11th Session of the FAO Conference and in 1963 by the 16<sup>th</sup> Session of the World Health Assembly. Revised in 1966 and 2006), in Codex Alimentarius Commission, Procedural Manual – Twenty-third edition, Rome, 2015, pp. 4-6.
- WTO, Agreement on the Application of Sanitary and Phytosanitary Measures, 15 April 1994, 1867 U.N.T.S. 493 (1994).
- WTO, Agreement on Technical Barriers to Trade, 15. April 15, 1994, 1868 U.N.T.S. 120 (1994).

#### INTERNATIONAL CASE LAW

- International Court of Justice, Reparations for Injuries Suffered in the Service of the United Nations Case ICJ (1949) ICJ Reports p. 174.
- WTO Appellate Body, United States – Measures Concerning the Importation and Marketing and Sale of Tuna and Tuna Products, WT/DS381/AB/R of 12 May 2012.

#### ICH MATERIALS

- ICH, Statement by the ICH Steering Committee Tokyo, October 1990, available at: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Vision/ICH\\_SC\\_Statement\\_1990.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Vision/ICH_SC_Statement_1990.pdf), last accessed: 3 April 2017.
- ICH, 'The Value and Benefits of ICH for Industry', January 2000, available via: <http://www.ich.org/ichnews/publications/browse/article/the-values-and-benefits-of-ich-to-industry.html>, last accessed: 3 April 2017.
- ICH, The Future of ICH – Revised 2000 – Statement by the ICH Steering Committee on the occasion of the Fifth International Conference on Harmonisation, 9-11 November 2000, San Diego, available via: [http://www.ich.org/fileadmin/-Public\\_Web\\_Site/ABOUT\\_ICH/Vision/The\\_Future\\_of\\_ICH\\_-\\_Revised\\_2000.pdf](http://www.ich.org/fileadmin/-Public_Web_Site/ABOUT_ICH/Vision/The_Future_of_ICH_-_Revised_2000.pdf), last accessed: 6 May 2015. (The information has now been removed from the website. A copy is on file with the author.)
- ICH, ICH Global Cooperation Group – Terms of Reference, November 2003, p.1, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Vision/GCG\\_-Statement\\_2003.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Vision/GCG_-Statement_2003.pdf), last accessed: 3 April 2017.

- ICH, Proceedings of the ICH Tokyo Symposium: Hot Topics and Influence on Asia – Tokyo 2007, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/E-ICH\\_Public\\_Meetings/ICH\\_Symposium\\_Tokyo\\_Japan\\_-\\_Nov\\_2\\_2007/Tokyo\\_Symposium\\_Proceedings\\_2007.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/E-ICH_Public_Meetings/ICH_Symposium_Tokyo_Japan_-_Nov_2_2007/Tokyo_Symposium_Proceedings_2007.pdf), last accessed: 3 April 2017.
- ICH, ICH Steering Committee May 5-10, 2007, Brussels Belgium – Summary, p. 8, available via: [http://www.ich.org/fileadmin/\\_migrated/content\\_uploads/SC\\_Report\\_Brussels\\_-2007.pdf](http://www.ich.org/fileadmin/_migrated/content_uploads/SC_Report_Brussels_-2007.pdf), last accessed: 3 April 2017.
- ICH, ICH Global Cooperation Group Meeting Report, Tuesday June 3, 2008, Portland, Oregon, USA, p. 2, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/C-GCG\\_Reports/June\\_2008\\_Portland\\_USA/-Final\\_GCG\\_Report\\_Portland\\_USA\\_June\\_2008.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/C-GCG_Reports/June_2008_Portland_USA/-Final_GCG_Report_Portland_USA_June_2008.pdf), last accessed: 3 April 2017.
- ICH, ‘The Value and Benefits of ICH to Drug Regulatory Authorities’, November 2010, available at: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/News\\_room/-C\\_Publications/ICH\\_20\\_anniversary\\_Value\\_Benefits\\_of\\_ICH\\_for\\_Regulators.pdf](http://www.ich.org/fileadmin/Public_Web_Site/News_room/-C_Publications/ICH_20_anniversary_Value_Benefits_of_ICH_for_Regulators.pdf), last accessed: 3 April 2017.
- ICH, Press Release – ICH Steering Committee, Fukuoka, Japan, 6-7 June 2012, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-fukuoka-japan-6-7-june-2012.html>, last accessed: 3 April 2017.
- ICH, Press Release – ICH Steering Committee, San Diego, USA, 14-15 November 2012, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-san-diego-ca-usa-14-15-november-2012.html>, last accessed: 3 April 2017.
- ICH, ICH Steering Committee, La Hulpe, Belgium, June 2013, Press Release, <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-la-hulpe-belgium-june-2013.html>, last accessed: 3 April 2017.
- ICH, Press Release – ICH Steering Committee, Osaka, Japan November 2013, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-osaka-japan-november-2013.html>, last accessed: 3 April 2017.
- ICH, Press Release – ICH Steering Committee, Minneapolis, MN, USA, June 2014, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-minneapolis-mn-usa-june-2014.html>, last accessed: 3 April 2017.
- ICH, Press Release – ICH Steering Committee, Lisbon, Portugal, December 2014, available via: <http://www.ich.org/ichnews/press-releases/view/article/ich-steering-committee-lisbon-portugal-november-2014.html>, last accessed: 3 April 2017.
- ICH, Press Release – ICH announces organisational changes as it marks 25 years of successful harmonisation, Geneva, 26 October 2015, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/News\\_room/B-Press\\_Releases/Press\\_Release\\_26Oct2015\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/News_room/B-Press_Releases/Press_Release_26Oct2015_Final.pdf), last accessed: 3 April 2017.
- ICH, Meeting Report ICH Assembly, Jacksonville, Florida, 9-10 December 2015, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/B-SC\\_Reports/-Assembly\\_report\\_Jacksonville\\_2015.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/B-SC_Reports/-Assembly_report_Jacksonville_2015.pdf), last accessed: 3 April 2017.
- ICH, ICH Procedures – Endorsed by the ICH Steering Committee on 10 June 2015, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/-Process\\_of\\_Harmonisation/ICH\\_Procedures\\_updated\\_July\\_2\\_2015.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/-Process_of_Harmonisation/ICH_Procedures_updated_July_2_2015.pdf), last accessed: 3 April 2017.
- ICH, Inaugural Assembly of the International Council For Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), 23 October 2015, Final Minutes, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/-ABOUT\\_ICH/Organisational\\_changes/ICH\\_Inaugural\\_Assembly\\_Minutes\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/-ABOUT_ICH/Organisational_changes/ICH_Inaugural_Assembly_Minutes_Final.pdf), last accessed: 3 April 2017.

ICH, Meeting Minutes ICH Assembly June 15-16 2016, Lisbon, Portugal, 20 September 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/-Ass\\_MC\\_Meetings\\_Reports/Assembly\\_report\\_Lisbon\\_2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/-Ass_MC_Meetings_Reports/Assembly_report_Lisbon_2016.pdf), last accessed: 3 April 2017.

ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Articles of Association, Adopted by the ICH Founding Members at ICH Inaugural Assembly on 23 October 2015, Approved by the Assembly 6 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_Articles\\_of\\_Association\\_for\\_Assembly\\_final\\_9Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_Articles_of_Association_for_Assembly_final_9Nov2016.pdf), last accessed: 3 April 2017.

ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Management Committee, Approved by the Management Committee on 16 June 2016, Last update approved by the Management Committee on 8 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_MC\\_RoPs\\_Approved\\_by\\_Assembly\\_final\\_8Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_MC_RoPs_Approved_by_Assembly_final_8Nov2016.pdf), last accessed: 3 April 2017.

ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Standard Operating Procedure of the ICH Working Groups, Version 2.0, Last update by the ICH Management Committee on 8 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_EWG\\_IWG\\_SOP\\_final\\_1Dec2016\\_Osaka\\_v2.0.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_EWG_IWG_SOP_final_1Dec2016_Osaka_v2.0.pdf), last accessed: 3 April 2017.

ICH, ICH Association 2017 Annual Work Plan, 10 November 2016, MC 2016/40, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Work\\_plans\\_Reports/ICH\\_Association\\_Work\\_Plan\\_2017\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Work_plans_Reports/ICH_Association_Work_Plan_2017_Final.pdf), last accessed: 3 April 2017.

ICH, ICH Association Multi-Annual Strategic Plan, 10 November 2016, MC 2016/40, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Work\\_plans\\_Reports/ICH\\_Association\\_Multi-Annual\\_Strategic\\_Plan\\_Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Work_plans_Reports/ICH_Association_Multi-Annual_Strategic_Plan_Nov2016.pdf), last accessed: 3 April 2017.

ICH, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – Rules of Procedure of the Assembly, Approved by the Assembly on 10 December 2015, Last update approved by the Assembly on 16 November 2016, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Articles\\_Procedures/ICH\\_Assembly\\_RoPs\\_Approved\\_by\\_Assembly\\_final\\_9Nov2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ICH_Assembly_RoPs_Approved_by_Assembly_final_9Nov2016.pdf), last accessed: 3 April 2017.

ICH, Meeting Minutes ICH Assembly November 9-10 2016, Osaka, Japan, 2 February 2017, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/Ass\\_MC\\_Meetings\\_Reports/Assembly\\_report\\_Osaka\\_2016.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/Ass_MC_Meetings_Reports/Assembly_report_Osaka_2016.pdf), last accessed: 3 April 2017.

ICH, ICH Association 2015 Annual Report, available via: [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ABOUT\\_ICH/Work\\_plans\\_Reports/2015\\_Annual\\_Report\\_ICH\\_Association\\_Final.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Work_plans_Reports/2015_Annual_Report_ICH_Association_Final.pdf), last accessed: 3 April 2017.

#### ICH GUIDELINES (IN ORDER OF ICH SYSTEMATISATION)

ICH, ICH Harmonised Tripartite Guideline – Stability Testing of New Drug Substances and Products Q1A(R2), 6 February 2003.

ICH, ICH Harmonised Tripartite Guideline – Stability Testing: Photostability Testing of New Substances and Products Q1B, 6 November 1996.

- ICH, ICH Harmonised Tripartite Guideline – Impurities In New Drug Substances Q3A(R2), 25 October 2006.
- ICH, ICH Harmonised Tripartite Guideline – Impurities In New Drug Products Q3B(R2), 2 June 2006.
- ICH, ICH Harmonised Tripartite Guideline – Impurities: Guideline For Residual Solvents Q3C(R5), 4 February 2011.
- ICH, ICH Harmonised Tripartite Guideline – Guideline For Elemental Impurities Q3D, 16 December 2014.
- ICH, ICH Harmonised Tripartite Guideline – Specifications: Test Procedures And Acceptance Criteria For New Drug Products: Chemical Substances Q6A, 6 October 1999.
- ICH, ICH Harmonised Tripartite Guideline – Specifications: Test Procedures And Acceptance Criteria For Biotechnological/Biological Products Q6B, 10 March 1999.
- ICH, ICH Harmonised Tripartite Guideline – Good Manufacturing Practice Guide For Active Pharmaceutical Ingredients Q7, 10 November 2000.
- ICH, ICH Harmonised Tripartite Guideline – Guideline On The Need For Carcinogenicity Studies of Pharmaceuticals S1A, 29 November 1995.
- ICH, ICH Harmonised Tripartite Guideline – Testing for Carcinogenicity Of Pharmaceuticals S1B, 16 July 1997.
- ICH, ICH Harmonised Tripartite Guideline – Dose Selection For Carcinogenicity Studies of Pharmaceuticals S1C(R2), 27 October 1994.
- ICH, ICH Harmonised Tripartite Guideline – Guidance On Genotoxicity Testing And Data Interpretation For Pharmaceuticals Intended For Human Use S2(R1), 9 November 2011.
- ICH, ICH Harmonised Tripartite Guideline – Detection of Toxicity To Reproduction For Medicinal Products & Toxicity To Male Fertility S5(R2), 24 June 1993.
- ICH, ICH Harmonised Tripartite Guideline – Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals S6(R1), 16 July 1997.
- ICH, ICH Harmonised Tripartite Guideline – The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life-Threatening Conditions (E 1), 27 October 1994.
- ICH, ICH Harmonised Tripartite Guideline – Clinical Safety Data Management: Definitions And Standards For Expedited Reporting E2A, 27 October 1994.
- ICH, ICH Harmonised Tripartite Guideline – Post-Approval Safety Data Management: Definitions And Standards For Expedited Reporting E2D, 12 November 2003.
- ICH, ICH Harmonised Tripartite Guideline – Ethnic Factors In The Acceptability For Foreign Clinical Data E5(R1), 5 February 1998.
- ICH, ICH Harmonised Tripartite Guideline – Guideline For Good Clinical Practice E6, 10 June 1996.
- ICH, ICH Harmonised Tripartite Guideline – General Considerations for Clinical Trials (E8), 17 July 1997.
- ICH, ICH Harmonised Tripartite Guideline – Statistical Principles for Clinical Trials (E9), 5 February 1998.
- ICH, ICH Harmonised Tripartite Guideline – Choice of Control Group and Related Issues in Clinical Trials (E10), 20 July 2000.
- ICH, Draft ICH Consensus Principle – Principles for Clinical Evaluation of New Antihypertensive Drugs E12A, 2 March 2000.
- ICH, ICH Tripartite Guideline – Organisation Of The Common Technical Document For The Registration Of Pharmaceuticals For Human Use M4, 5 June 2016.

- ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Quality – M4Q(R1) – Quality Overall Summary Of Module 2 And Module 3: Quality, 12 September 2002.
- ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Safety – M4S(R2) – Overview And Nonclinical Summaries Of Module 2 – Organisation Of Module 4, 20 December 2002.
- ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Safety – M4S(R2) – Overview And Nonclinical Summaries Of Module 2 – Organisation Of Module 4, 20 December 2002.
- ICH, ICH Tripartite Guideline – The Common Technical Document For The Registration Of Pharmaceuticals For Human Use: Efficacy – M4E(R2) – Overview And Clinical Summary Of Module 2- Module 5 Clinical Study Reports, 15. June 2016.

#### OTHER DOCUMENTS

- International Labour Organisation, ILO Constitution, available via: [http://www.ilo.org/dyn/normlex/en/f?p=1000:62:0::NO:62:P62\\_LIST\\_ENTRIE\\_ID:2453907:NO](http://www.ilo.org/dyn/normlex/en/f?p=1000:62:0::NO:62:P62_LIST_ENTRIE_ID:2453907:NO), last accessed: 3 April 2017.
- International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), Organisational Charter of VICH, VICH/96/002 Revision 13, October 2016 FINAL.
- International Organisation for Standardization, ISO Statutes, 17th Edition, 2013.
- OECD, OECD Series on Testing and Assessment Number 1 – Guidance Document for the development of OECD Guidelines for the testing of chemicals (as revised 2009), 5 Aug 2009, ENV/JM/MONO(2006)20/REV1.
- WHO, ‘International Harmonization of Regulatory Activities: Future Options’, 14(3) WHO Drug Information (2000).
- WHO, ‘The Impact of Implementation of ICH Guidelines in Non-ICH Countries’, Regulatory Support Series No. 009, 2002, available via: <http://apps.who.int/medicinedocs/en/d/Jh2993e/>, last accessed: 3 April 2017.
- United Nations, Report of the Secretary-General – Enhanced Cooperation between the United Nations and All Relevant Partners, in Particular the Private Sector, A/60/214, 10 August 2005.

#### NATIONAL LAW

- Swiss Civil Code of 10 December 1907, Status as of 1 January 2017.
- UK, Sale of Food and Drugs Act 1874.
- US, Federal Food and Drugs Act 1906.

#### NEWSPAPER ARTICLES

- C. Briseño, ‘Skandal-Medikament Avandia: Diabetes-Blockbuster droht das Aus, Der Spiegel, 07.09.2010; available via: <http://www.spiegel.de/wissenschaft/medizin/skandal-medikament-avandia-diabetes-blockbuster-droht-das-aus-a-715917.html>, last accessed: 3 April 2017.
- Euractiv, ‘Brussels seeks to simplify rules on clinical trials’, 18 July 2012, available via: <http://www.euractiv.com/health/brussels-vows-simplify-clinical-news-513975>, last accessed: 3 April 2017.

- Euractiv, 'MEP's give resounding 'yes' to new clinical trials rules', 30 Mai 2013, available via: <http://www.euractiv.com/health/meps-clinical-trials-need-clear-news-528127>, last accessed: 3 April 2017.
- Euractiv, 'Why Juncker should backtrack and keep pharma policy in the health portfolio', 18 September 2014, available via: <http://www.euractiv.com/sections/health-consumers/why-juncker-should-backtrack-and-keep-pharma-policy-health-portfolio>, last accessed: 3 April 2017
- Euractiv, 'Juncker turn puts pharma in health Commissioner portfolio', 22 October 2014, available via: <http://www.euractiv.com/sections/health-consumers/juncker-u-turn-puts-pharma-health-commissioners-portfolio-309396>, last accessed: 3 April 2017.
- Euractiv, 'A bad start for the new Commission', 11 September 2015, available via: <http://www.euractiv.com/sections/health-consumers/bad-start-new-commission-308376>, last accessed: 3 April 201
- European Public Health Alliance, MEPs support health community call for Health Commissioner to 'own' pharmaceutical policy, available via: <http://v3.eph.org/spip.php?article3542>, last accessed: 3 April 2017.
- European Public Health Alliance, [Open letter] To President-elect Jean Claude Juncker on move of medicinal products and health technologies to the portfolio of the Commissioner for internal market and industry, 16 September 2014, available via: <https://eph.org/open-letter-to-president-elect-jean-claude-juncker-on-move-of-medicinal-products-and-health-technologies-to-the-portfolio-of-the-commissioner-for-internal-market-and-industry>, last accessed: 3 April 2017.

## WEBSOURCES

[www.cioms.ch](http://www.cioms.ch)  
[www.consilium.europa.eu](http://www.consilium.europa.eu)  
[www.ec.europa.eu](http://www.ec.europa.eu)  
[www.echa.europa.eu](http://www.echa.europa.eu)  
[www.edqm.eu](http://www.edqm.eu)  
[www.ema.europa.eu](http://www.ema.europa.eu)  
[www.fao.org](http://www.fao.org)  
[www.hc-sc.gc.ca](http://www.hc-sc.gc.ca)  
[www.ich.org](http://www.ich.org)  
[www.ifpma.org](http://www.ifpma.org)  
[www.ilo.org](http://www.ilo.org)  
[www.iso.org](http://www.iso.org)  
[www.ipec.org](http://www.ipec.org)  
[www.i-p-r-f.org](http://www.i-p-r-f.org)  
[www.meddra.org](http://www.meddra.org)  
[www.oecd.org](http://www.oecd.org)  
[www.ombudsman.europa.eu](http://www.ombudsman.europa.eu)  
[www.regulations.gov](http://www.regulations.gov)  
[www.swissmedic.ch](http://www.swissmedic.ch)  
[www.usp.org](http://www.usp.org)



## Curriculum Vitae

Sabrina Röttger-Wirtz was born on 14 July 1987 in Aachen (Germany). She holds a bachelor degree (LL.B.) in European Law awarded by Maastricht University in 2008. Moreover, she obtained two LL.M. degrees in European Law (cum laude) and Globalisation & Law (cum laude) from Maastricht University in 2010. During her master studies she has been a student editor at the Maastricht Journal of European and Comparative Law. After her studies she joined the Legal Service of the European Medicines Agency as Trainee and later as Contract Agent until 2011. The research for this PhD thesis was carried out at Maastricht University, where Sabrina Röttger-Wirtz worked as a PhD Researcher and Lecturer in the Department of International and European Law from 2011 until 2017. Since September 2017, she works as Assistant Professor of EU Health Law at the Tilburg Institute for Law, Technology, and Society (TILT) at Tilburg University.