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**The Role of Domestic Administrative Law in the  
Accountability of Transnational Regulatory Networks:  
The Case of the ICH**

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# **The Role of Domestic Administrative Law in the Accountability of Transnational Regulatory Networks: The Case of the ICH**

*Ayelet Berman*<sup>1</sup>

## **Abstract**

The literature on the accountability of transnational regulatory networks (TRNs) has focused on accountability measures that are available at the transnational level. This paper extends the analysis and examines the role domestic administrative law has to play in keeping TRNs accountable towards their internal and external stakeholders. To this end it conducts a case study of the International Conference on Harmonization (ICH), a network of drug regulatory authorities and industry associations that harmonizes drug registration rules, and examines it primarily from a U.S. administrative law perspective. The paper, first, demonstrates that domestic administrative law can have an important role in setting the procedural rules of TRNs. Second, it shows that domestic administrative law is important in maintaining the accountability of TRNs and regulators towards internal stakeholders (i.e. stakeholders within member countries), but that it has limitations that should ideally be complemented by accountability measures at the transnational level. The paper, third, demonstrates that although theoretically domestic administrative law could play an important role in setting off the TRNs' disregard towards the interests of external stakeholders (stakeholders that are not network members), in practice this comes across serious problems. Accountability towards external stakeholders is, hence, best achieved through accountability measures at the transnational level.

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## 1. Introduction

Cooperation amongst regulatory authorities, or “transgovernmental regulatory networks” (or “transnational” when in collaboration with private actors)<sup>2</sup> (TRNs) has been prevalent in the past two decades, in diverse areas such as finance, competition, and environmental issues. Despite the many benefits of such networking, a lot of the scholarly work on TRNs has been concerned with their accountability deficits, and various claims have been made. They have been said to lack transparency.<sup>3</sup> They have been criticized for their “club-like” nature – dominated by the US and Europe while affecting third countries, particularly developing countries, which do not adequately participate in their procedures.<sup>4</sup> Moreover, it has been argued that affected nongovernmental actors are not sufficiently involved.<sup>5</sup> Another frequent charge against TRNs has been that they are networks of unconstrained technocrats, or “agencies on the loose”,<sup>6</sup> the main concern being the lack of domestic political or legal control over the bureaucracy,<sup>7</sup> and the shifting of the decision making away from accessible, accountable national government to international bodies that are inaccessible to citizens.<sup>8</sup>

While most of the accountability literature has focused on the accountability measures available at the global level,<sup>9</sup> this paper seeks to expand the analysis by examining the role domestic administrative law and practice (in short, domestic administrative law) has to play in the accountability of TRNs (whether purely public or public-private). The focus is on TRNs that are in the business of

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<sup>2</sup> Anne-Marie Slaughter, *A New World Order* (Princeton University Press, Princeton 2004).

<sup>3</sup> Robert O. Keohane, 'Global Governance and Democratic Accountability' (Miliband Lectures, London School of Economics 2002) <<http://www2.lse.ac.uk/publicEvents/pdf/20020701t1531t001.pdf>> accessed 11 October 2011.

<sup>4</sup> David Zaring, 'Informal Procedure, Hard and Soft, in International Administration' (2005) 5 *Chicago Journal of International Law* 547, 595.

<sup>5</sup> Mario Savino, 'An Unaccountable Transgovernmental Branch: The Basel Committee' in S. Cassese et al. (eds.), *Global Administrative Law: Cases, Materials, Issues* (Institute for International Law and Justice: NYU School of Law, and Istituto di Ricerche sulla Pubblica Amministrazione 2008)69.

<sup>6</sup> A.M. Slaughter, 'Agencies on the loose? Holding government networks accountable' (2000) [http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=209319](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=209319), accessed 11 October 2011.

<sup>7</sup> Benedict Kingsbury, Nico Krisch, and Richard B. Stewart, 'The Emergence of Global Administrative Law' (2005) 68 *Law and Contemporary Problems* 15, 16; Karl Kaiser, 'Transnational Relations as a Threat to the Democratic Process' (1971) 25 *International Organization* 706, 717-719; Jan Klabbers, *An Introduction to International Institutional Law* (Cambridge University Press, Cambridge 2002) 339.

<sup>8</sup> Lori M. Wallach, 'Accountable Governance in the Era of Globalization: The WTO, NAFTA, and the International Harmonization of Standards' (2001-2002) 5 *University of Kansas Law Review* 823, 833.

<sup>9</sup> With several exceptions: R.B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' (2005) 37 *New York University Journal of International Law and Politics* 695, P.H. Verdier, 'Transnational Regulatory Networks and Their Limits' (2009) 34 *Yale J. Int'l L.* 113, Pierre-Hugues Verdier, 'U.S. Implementation of Basel II: Lessons for Informal International Law-Making (Draft Paper)' (Informal International Law Making Workshop, Graduate Institute of International and Development Studies, Geneva 2010)

harmonizing rules or issuing standards or other normative output such as guidelines, best practices, recommendations etc. (generally referred to as “harmonization networks” in this paper).

In assessing the role of domestic administrative law in the accountability of harmonization networks, the paper develops an analytical framework, which it applies to a case study of the International Conference on the Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) examined from a US administrative law perspective. The paper draws lessons from this case for the general debate on the accountability of harmonization networks. The ICH is a network of drug regulatory authorities and industry associations from the US, EU and Japan, that harmonizes the technical requirements of drug registration rules.

The ICH is only one (even if the most significant) of a group of similar harmonization networks that deal with the harmonization of registration rules for health products. The other networks in this group are also characterized by a core membership of medical regulatory authorities and industry associations from the US, EU, Japan (and Canada and/or Australia in some cases). These other networks are the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH) (dealing with veterinary drugs),<sup>10</sup> the Global Harmonization Task Force (GHTF) (dealing with medical devices),<sup>11</sup> and the International Cooperation on Cosmetics Regulation (ICCR) (dealing with cosmetics).<sup>12</sup> Since the membership, the structure and the harmonization process of these networks are almost identical to that of the ICH, where relevant, the paper refers to them too.

The question as to how to keep these or similar harmonization networks accountable will become more important. Collaboration amongst regulators and their foreign counterparts, including towards harmonization of standards, is a central building block in the FDA’s strategy for the 21<sup>st</sup> century.<sup>13</sup> With globalization and the shift of supply chains to third countries, ascertaining their safety and integrity is a top FDA priority,<sup>14</sup> and the FDA has explicitly defined that collaboration with foreign counterparts, including towards harmonization, is central in achieving this goal. The FDA’s approach spearheads a global trend. The European Medicines Agency (EMA) has also put collaboration with foreign regulators as a central element of its international strategy, and other regulatory

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<sup>10</sup> <http://www.vichsec.org/> accessed 11 October 2011.

<sup>11</sup> [www.ghrf.org](http://www.ghrf.org). accessed 11 October 2011.

<sup>12</sup> <http://www.fda.gov/InternationalPrograms/HarmonizationInitiatives/ucm114513.htm>. accessed 11 October 2011.

<sup>13</sup> US Food and Drug Administration, 'Pathway to Global Product Safety and Quality' (2011) <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OC/GlobalProductPathway/UCM262528.pdf> accessed 11 October 2011.

<sup>14</sup> FDA, 'Strategic Priorities 2011-2015: Responding to the Public Health Challenges of the 21<sup>st</sup> Century' (2011) <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM252092.pdf> accessed 11 October 2011, p. 8.

agencies are following.

Moreover, the relevance of the accountability of harmonization networks goes much beyond the health sector: The alignment of diverging technical or social regulations, or what has been termed “3<sup>rd</sup> generation barriers to trade,”<sup>15</sup> is nowadays high on the trade liberalization agenda of market oriented economies. OECD and APEC members are explicitly encouraged to strengthen regulatory cooperation to harmonize standards,<sup>16</sup> with many initiatives already underway (for example between the US and Europe,<sup>17</sup> or US-Canada-Mexico,<sup>18</sup> to name just a few.) Collaboration with the private sector to this end, is considered important too.

While this paper focuses on the ICH/US law as a case study, the analytical framework proposed, and the specific conclusions can serve our analysis of any other harmonization network say in the financial, environmental etc. field (e.g. the Basel Committee on Banking Supervision). This paper argues that domestic law is significant in establishing the accountability of harmonization networks towards internal stakeholders, and has some role to play, albeit limited, in offsetting the problem of disregard towards external stakeholders. Transnational accountability measures are critical for external accountability, but also important in improving the accountability towards internal stakeholders. Domestic and transnational measures are, accordingly, complementary, and harmonization networks should be designed with this in mind.

The paper is organized as follows. Section 2 sets out the analytical framework of this paper. Section 3 provides a short overview of the ICH, and sets out several ICH specific accountability concerns. Section 4 concerns the role of domestic law in setting procedural rules for the network, and in limiting the topics negotiated at the transnational level. Section 5 concerns the role domestic law has in maintaining the accountability of the FDA, and in turn the network in its entirety, towards internal stakeholders. To this end, it addresses the domestic law that regulates transnational harmonization (5A), the accountability mechanisms (5B) and “other responsiveness promoting measures” (5C). Section 6 concerns the role domestic law has to play in the accountability of the network towards external

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<sup>15</sup> Mauro Petriccione, 'Reconciling Transatlantic Regulatory Imperatives with Bilateral Trade' in G. Bermann, M. Herdegen, and P. Lindseth (eds.), *Transatlantic Regulatory Cooperation: Legal Problems and Political Prospects* (Oxford University Press, Oxford/New York 2001).

<sup>16</sup> e.g. Principle 6 in OECD, 'The OECD 2005 Guiding Principles for Regulatory Quality and Performance' (2005) <http://www.oecd.org/dataoecd/19/51/37318586.pdf> accessed 11 Oct. 2011.

<sup>17</sup> e.g. United States Trade Representative (USTR), '2005 Roadmap for U.S and EU Regulatory Cooperation and Transparency' (2005) [http://www.ustr.gov/archive/World\\_Regions/Europe\\_Middle\\_East/Europe/US\\_EU\\_Regulatory\\_Cooperation/2005\\_Roadmap\\_for\\_EU-US\\_Regulatory\\_Cooperation\\_Transparency.html](http://www.ustr.gov/archive/World_Regions/Europe_Middle_East/Europe/US_EU_Regulatory_Cooperation/2005_Roadmap_for_EU-US_Regulatory_Cooperation_Transparency.html) accessed 11 Oct. 2011.

<sup>18</sup> 'Canada/United States/Mexico Security and Prosperity Regulatory Cooperation Framework' (2005) [http://www.spp-psp.gc.ca/eic/site/spp-psp.nsf/vwapj/RCF-eng.pdf/\\$FILE/RCF-eng.pdf](http://www.spp-psp.gc.ca/eic/site/spp-psp.nsf/vwapj/RCF-eng.pdf/$FILE/RCF-eng.pdf) accessed 11 Oct. 2011.

stakeholders. Following a short introduction of the main external stakeholders (6A) and the main transnational accountability measures (6B), it distinguishes between domestic law in member countries (6C) and in non-member countries (6D). Section 7 concludes.

## 2. Defining the Analytical Framework for Accountability

This paper does not go into the vast literature on the definition of accountability. It adopts as its analytical framework a broad definition, namely an actor's "responsiveness", or rather "disregard", to the interests of others.<sup>19</sup> As regards these "others", or whom the actor should be accountable to, the paper presumes a distinction between the actors' accountability towards "internal" and "external" stakeholders. The first is based on a principal-agent relationship, and is between the actor and those that authorized the actor's activity. The second is between the actor and those affected by its actions.<sup>20</sup> The paper further relies on the distinction between (i) decision rules (i.e., who are the voting members), (ii) accountability mechanisms (i.e., procedures whereby specified account holders have the authority to hold specified power holders to give account for their conduct and impose sanctions or secure other remedies for deficient performance or unlawful conduct), and (iii) other responsiveness promoting measures (in particular transparency, and non-decisional participation).<sup>21</sup> The paper henceforth refers to all of these collectively as "accountability measures".

In thinking about the accountability of the ICH, or any other harmonization network, there are two main concerns: The first concern is the accountability of the network towards the *internal stakeholders*. The internal stakeholders are the governments behind the member regulatory authorities, and the companies behind the industry associations. Moreover, within each member country we have the businesses regulated by the networks' output, and the individuals and other diffused social interests within the member country affected by the output. Based on a formal principal-agent model of democracy, and to maintain analytical clarity, the paper considers such nongovernmental stakeholders within member countries to be internal stakeholders. The second concern is of the accountability/disregard of the network towards its *external stakeholders*. External stakeholders are non-member countries that adopt a network's guidelines. Business or diffused social interests affected by the network's output

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<sup>19</sup> Richard B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper )' (IILJ International Legal Theory Colloquium: Interpretation and Judgment in International Law, NYU Law School 2008) <<http://www.iilj.org/courses/documents/2008Colloquium.Session4.Stewart.pdf>>, Joost Pauwelyn, 'Informal International Law-Making: Mapping the Action and Testing Concepts of Accountability and Effectiveness: Project Framing Paper' (Informal International Law Making Workshop Graduate Institute of International and Development Studies, Geneva 2010)

<sup>20</sup> Ruth W. Grant and Robert O. Keohane, 'Accountability and Abuses of Power in World Politics' (2005) 99 *American Political Science Review* 29, 31.

<sup>21</sup> J. Pauwelyn, 'Informal International Law-Making: Mapping the Action and Testing Concepts of Accountability and Effectiveness: Project Framing Paper' , R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper )' .



(but not represented by the network members) fall into this category too. These may be from non-member states, and in some cases transnational actors (such as industry associations or patients organizations whose members come from both member and non-member countries). In our analysis of the accountability of harmonization networks, we must, accordingly, examine the accountability measures that exist towards the internal and towards the external stakeholders.



[Graphic: The ICH's Internal and External Stakeholders]

In dealing with these two problems, we can think of a TRN as an *actor* with a specific organizational form that can be contrasted with markets or hierarchies (say a treaty based intergovernmental organization),<sup>22</sup> or we can think of it as *interconnected nodes* (in this case, of national regulatory authorities and industry associations). Most of the scholarly debate concerning the accountability and legitimacy of TRNs (or of other global actors in general) has focused on accountability measures at the “actor”, or the transnational level. Such an analysis is clearly relevant and important. The purpose of this paper, however, is to contribute by zooming in on the “node”, or the regulatory authority, and to check, empirically, the role domestic law is playing and could play, in the accountability of the regulatory authorities, and in turn, of the network as a whole, towards its

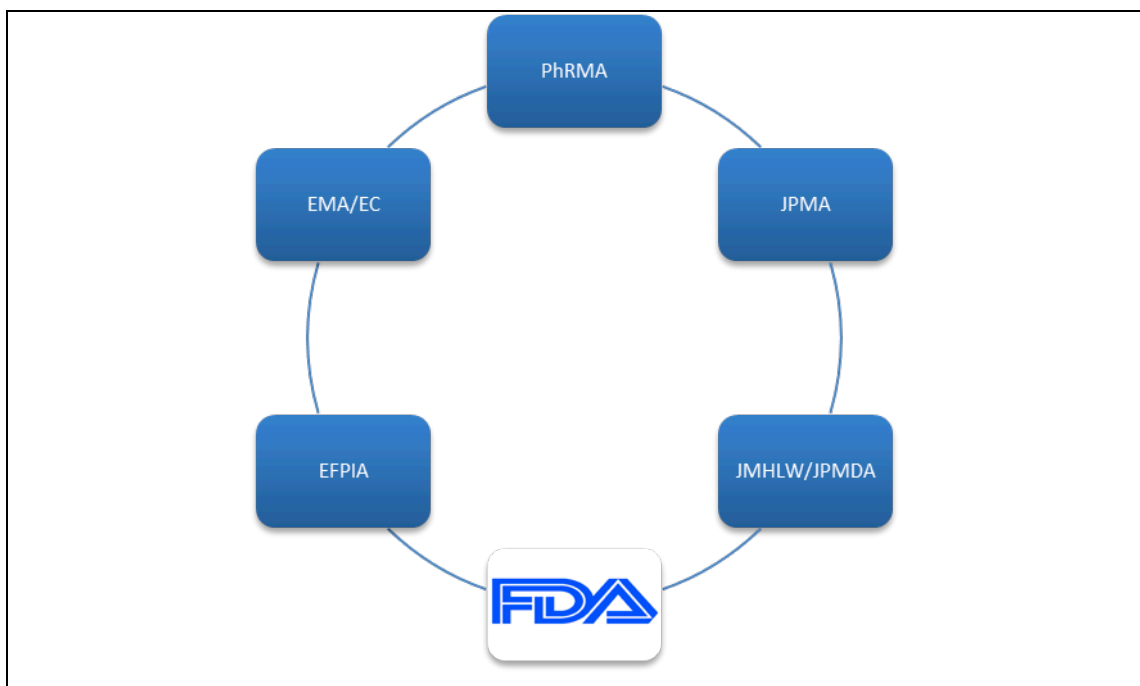
<sup>22</sup> Walter W. Powell, 'Neither Market Nor Hierarchy: Network Forms of Organization' (1990) 12 *Research in Organizational Behavior* 295, , Miles Kahler, *Networked Politics: Agency, Power and Governance* (Cornell Studies in Political Economy, Cornell University Press, 2009) 4-5.

internal and external stakeholders.

Hence, in our analysis of accountability, it is helpful to divide the process into two levels and to examine the accountability measures (towards internal and external stakeholders) that exist in each:

1. Accountability measures at the “**Transnational**” Level (TRN as an **Actor**).
2. Accountability measures at the “**Domestic**” Level (TRN as comprised of interconnected **Nodes**).

In practice there is some overlap, but for analytical purposes this division is helpful. A proper analysis of accountability of any TRN would have to examine accountability measures at both levels. In this paper, we only explore the role of the domestic level. That is, we suggest a way to explore the accountability measures towards internal and external stakeholders that exist at the domestic level.



*[Graphic: The ICH as an actor or as interconnected nodes.]*

Anne Marie Slaughter is the scholar to have made most notably the case of solving the accountability problems of TRNs through boosting domestic

accountability procedures.<sup>23</sup> Since TRNs are composed of regulators, which in turn are bound by domestic administrative law, this avenue of research indeed strikes as promising. This paper, accordingly, explores this possibility, focusing on the current legal situation in the US. While Slaughter's work focused on purely transgovernmental networks, the question is equally relevant where regulators collaborate with private actors, such as in the ICH, GHTF, VICH, ICCR and so forth.

Finally, in his seminal work, Robert Putnam made the point that the politics of many international negotiations can be conceived as a "two-level game". That is, that while national negotiators appear at the international table with their foreign counterparts, they have the "domestic" table, with all domestic stakeholders, behind them and there are crucial links and counterinfluences between the "games" of each level.<sup>24</sup> One of the central arguments of his model is that domestic preferences, coalitions and institutions determine the domestic implementability of an international agreement, and in turn, affect and limit the bargaining and decision making at the international level. This paper is very much in line with Putnam's argument and seeks to provide insight on the impact domestic administrative law has on the accountability of the transnational bargaining process.

Before proceeding with this analysis, the next section provides a short overview of the ICH.

### **3. Background on the ICH**

#### ***a. ICH Overview***

The ICH was set up two decades ago, and is composed of drug regulatory authorities and R&D pharmaceutical industry associations (i.e. industry dealing with the development of *new* drugs) from the US, EU and Japan. The public parties are the US Food and Drug Administration (FDA), the European Commission DG Health and Consumers, the European Medicines Agency (EMA), the Japanese Ministry of Health, Labor & Welfare (MHLW) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA). The private parties are the Pharmaceutical Research & Manufacturers Association of America (PhRMA), the European Federation of Pharmaceutical Industries' Associations (EFPIA) and the Japanese Pharmaceutical Manufacturers Association (JPMA). Certain observers and private interested parties may attend too, such as the WHO, Swissmedic (the Swiss drug regulator) on behalf of EFTA countries, Health Canada, or the International Generic Pharmaceuticals Alliance ([IGPA](#)) (as well as other ad hoc observers). The Secretariat is run by the International Federation of

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<sup>23</sup> A.-M. Slaughter, *A New World Order*, 218. Anne-Marie Slaughter and David Zaring, 'Networking Goes International: An Update' (2006) 2 Annual Review of Law and Social Science 211, 222.

<sup>24</sup> Robert D. Putnam, 'Diplomacy and Domestic Politics: The Logic of Two Level Games' (1988) 42 International Organization 427, 434.

Pharmaceutical Manufacturers and Associations (IFPMA).<sup>25</sup>

The purpose of the ICH is to harmonize the technical requirements of drug registration rules concerning the quality, efficacy and safety of drugs between its member countries, but in practice many of its standards have become global standards adopted by a wide range of countries. It works in expert working groups (EWGs) and a Steering Committee (SC), in which industry and regulators have an equal number of seats and decisions are reached by way of consensus. It issues legally non-binding guidelines, which are in most cases adopted as nationally legally non-binding rules (FDA “guidance document”/EMA “guidelines”).

### ***b. Main Concerns***

There are two main effects of the ICH process that have caught the attention of critics and that raise particular interest from an accountability perspective.

First, criticism has been raised that the industry dominates the ICH and that this undermines public health interests. The main claim in this context has been that some of the safety and efficacy guidelines promote faster and cheaper drug development to the benefit of industry but at the cost of patient security.<sup>26</sup>

Second, while the ICH’s guidelines were initially intended for the US, Europe and Japan, many of its guidelines have now become *de facto* global standards, adopted worldwide. One of the main concerns in this context has been that its standards for assuring the quality of drugs are technology driven and “unnecessarily” high in the sense that they increase manufacturing costs without providing any public health benefits. Big pharmaceutical companies absorb such costs relatively easily, but smaller companies, in particular in developing countries and those producing generic medicines, can’t afford them. This in turn, the WHO and several NGOs have claimed, may lead to a squeeze out of local producers and to reduced access of the local population to essential medicines.<sup>27</sup>

A related concern has been that guidelines on clinical trials are also not sensitive to local needs in developing countries, leading to a dangerous decline in clinical trials in such countries.<sup>28</sup>

What role then have domestic administrative law procedures had in providing accountability in these two cases? What role could they have in future cases? Sections 5 and 6 of this paper will provide more answers in this respect.

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<sup>25</sup> See [www.ich.org](http://www.ich.org) accessed 11 Oct. 2011.

<sup>26</sup> See John Abraham, 'The Pharmaceutical Industry as a Political Player' (2002) *The Lancet* 1498, Prescrire, 'ICH: An Exclusive Club of Drug Regulatory Agencies and Drug Companies Imposing its Rules on the Rest of the World' (2010) 19 *Prescrire International* 183, 184-185.

<sup>27</sup> WHO, 'Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries' (Geneva 13-15 September 2001) <http://apps.who.int/medicinedocs/pdf/h2993e/h2993e.pdf>, WHO, 'Global Harmonization and the ICH' *Essential Drugs Monitor* (2001) <http://apps.who.int/medicinedocs/en/d/Jh2977e/4.html>, accessed , Prescrire, 'ICH: An Exclusive Club of Drug Regulatory Agencies and Drug Companies Imposing its Rules on the Rest of the World'

<sup>28</sup> Trudie Lang, Phaik Yeong Cheah, and Nicholas J. White, 'Clinical research: time for sensible global guidelines' (7 May 2011) 377 *The Lancet* 1553, 1555.

Beforehand, in the following section, we examine the role domestic law and practice has in setting good administrative practices and in determining the topics deliberated and harmonized at the transnational level.

#### 4. Domestic Administrative Law and the Transnational Level

##### a. *Accountability Measures*

In the US it has been a long-standing approach to encourage the participation of federal agencies in standard-setting activities outside of the government (whether domestic/international, or private/public). This approach was first set out in OMB Circular A-119 “Federal Participation in the Development and Use of Voluntary Consensus Standards and in Conformity Assessment Activities”, that has been issued several times, dating back to the 1970s. The “National Technology Transfer and Advancement Act”, issued in 1995, codifies the Circular. Following and based on the Circular and NTTAA, the FDA issued three FDA- specific regulations and policies that regulate its participation in outside standard-setting activities and apply to its participation in the ICH. The binding regulation on “Participation in outside standard-setting activities,”<sup>29</sup> the “Policy on the development and use of standards with respect to international harmonization of regulatory requirements and guidelines,”<sup>30</sup> and the Staff Manual Guide 9100.1 “Development and Use of Standards.”<sup>31</sup>

These FDA-specific rules set out, *inter alia*, minimum *procedural* requirements with which the *outside* standard setting activity must conform, in order for FDA employees to be allowed to participate. The regulation demands that a private standard-setting activity in which FDA employees participate, “(ii) will not be designed for the economic benefit of any company, group, or organization...and (iii) that the group or organization responsible for the standard-setting activity must have a procedure by which an interested person will have an opportunity to provide information and views on the activity and standards involved, without the payment of fees, and the information and views will be considered.”<sup>32</sup> The Policy similarly determines that the activity’s “development process for the standard is transparent (i.e., open to public scrutiny), comply with applicable statutes, regulations, and policies, specifically including §10.95 and OMB Circular A-119, and is consistent with the codes of ethics that must be followed by FDA employees”.<sup>33</sup> The Policy also sets out *substantive*

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<sup>29</sup> 21 CFR 10.95.

<sup>30</sup> FDA, 'International Harmonization: Policy on Standards (Notice)' 60 Federal Register 53078 (11 October 1995) .

<sup>31</sup> FDA, 'Staff Manual Guide 9100.1: Common Standards, Development and Use of Standards' (22 May 2007) <http://www.fda.gov/AboutFDA/ReportsManualsForms/StaffManualGuides/ucm193332.htm> accessed at 11. Oct. 2011.

<sup>32</sup> 21 CFR 10.95 (d)(5)

<sup>33</sup> FDA 'International Harmonization: Policy on Standards (Notice)' (11 October 1995), s. IV(A)(3).

requirements, such as that “the harmonization activity should be *consistent with U.S. Government policies* and procedures and should promote U.S. interests with foreign countries” and that “the harmonization activity should further FDA’s mission to protect the *public health*.”<sup>34</sup>

While the US acknowledged the advantages attached to governmental collaboration with private actors in standard setting, it was equally understood that such collaboration raises concerns about regulatory capture and the necessity to safeguard the public interest.<sup>35</sup> These rules were hence introduced so as to encourage compliance with public interest safeguards, and to bring the FDA’s (and other US agencies) outside standard-setting activities in line with national norms of transparency, participation and accountability. When setting up the ICH, the FDA insisted on inclusion of safeguards in line with these rules. The idea underlying this demand was that transparency, participation, due process, ethics standards etc. would shield the process from inappropriate industry influence, and would guard the integrity of the scientific-based process. Moreover, the very fact that regulators participate was also considered a safeguard of the public interest.

It is often claimed that TRNs fall in the cracks between domestic and international law.<sup>36</sup> But since US federal agencies may only (at least formally) participate in such outside standard-setting activities that comply with procedural requirements of transparency and participation, and in view of the FDA’s dominance in drug registration, the FDA has the power to unilaterally impose good administrative practices on the network. Hence, while US law does not *de jure* apply to the network, it may do so *de facto*. This is a “bottom up” approach of extending US administrative law to global procedures.<sup>37</sup> Moreover, if other countries adopt similar rules, in particular powerful members such as the EU, then such requirements will further impose themselves on TRNs. More generally, it can be concluded that a network may be *de facto* bound by the domestic legal requirements of its most dominant participants.

In practice, good administrative practice is often extended “bottom up” by the regulators to their transnational activities without any specific obligation set out in their domestic laws but as a reflection of the nature of their domestic practices. For instance, at the EC’s initiative, the ICCR, without any legal obligation to do so, recently convened a first ever ICCR stakeholders meeting at which industry, patient and animal protection NGOs voiced their views and requests.<sup>38</sup>

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<sup>34</sup> Ibid. s. I(B)(1).

<sup>35</sup> See generally, Walter Mattli, 'Public and Private Governance in Setting International Standards' in M. Kahler and D. A. Lake (eds.), *Governance in a Global Economy: Political Authority in Transition* (Princeton University Press, 2003) 200.

<sup>36</sup> HiiL, 'Tender Document: Democracy and Accountability in the Context of Informal International Public Policy-Making' (2008) [http://www.hiil.org/assets/204/HIIL\\_n6434\\_v21\\_HiiL\\_Constitutional\\_Law\\_Project\\_-\\_Tender\\_Document.pdf](http://www.hiil.org/assets/204/HIIL_n6434_v21_HiiL_Constitutional_Law_Project_-_Tender_Document.pdf) accessed 11.Oct.2011.

<sup>37</sup> R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 753-754.

<sup>38</sup> Laurent Selles (EC Health and Consumers DG), 'Announcement of ICCR-5 Stakeholder Session in Paris, June 30, 2011' (2011)

The point to take from here is that in ensuring good administrative practice at the transnational level, powerful countries such as the US and EC should determine conditions in their laws that would bind regulators in their transnational activities, and would in turn bind the network. In the absence of any international agreements on such topics, such “bottom up” insistence on good administrative practices would be the most efficient way to achieve this goal.

Finally, as international liberal IR theory would predict,<sup>39</sup> also domestic accountability mechanisms that go beyond domestic legal requirements may influence the network’s structure. While this topic is beyond the scope of this paper, it is worth noting that following criticism by media and other sources in the US that regulators are too close to industry,<sup>40</sup> the FDA’s Commissioner instructed to stop the GHTF’s industry membership. The GHTF had been a regulators-industry network similar in structure to the ICH, and following this decision has very recently become a regulators only network. Rather than domestic legal mechanisms, reputational accountability mechanisms came into play here.<sup>41</sup>

### ***b. Topic Selection***

The results of this study suggest that domestic administrative practice significantly limits the range of topics deliberated and harmonized at the transnational level.

In all of the multilateral harmonization networks in which the FDA, EC and Japanese Ministry collaborate (ICH, VICH, GHTF, ICCR), topic selection at the transnational level is limited by three main preconditions. The network addresses only topics that fulfill these preconditions. The first condition is that the domestic implementation of the guideline will not require an amendment of binding laws or regulations in *any* of the member jurisdictions. The network will hence only deal with topics that can be implemented as domestically legally non-binding “guidance documents” or “guidelines”. For example, the ICH does not deal with the labeling of pharmaceuticals, despite it being a very attractive topic for harmonization, as it would require a domestic amendment of binding rules. Similarly, labeling of nano materials is off the table at the ICCR as the EC has already issued binding regulations on this topic.

This limitation also restricts power politics within the network. While the US and the EC are the most dominant members and Japan and others (e.g., Australia and Canada in the GHTF or ICCR) followers, the network respects such limitation

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[http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/iccr\\_june2011\\_en.pdf](http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/iccr_june2011_en.pdf) accessed 11. Oct. 2011.

<sup>39</sup> Andrew Moravcsik, 'Taking Preferences Seriously: A Liberal Theory of International Politics' (1997) 51 *International Organization* 513.

<sup>40</sup> John Wilkinson and John Brennan, 'The Future of the GHTF: Growing Pains Ahead?' *Scrip Regulatory Affairs* (10 May 2011) <http://www.rajpharma.com/productsector/medicaldevices/The-future-of-the-new-GHTF-growing-pains-ahead-315334>, accessed 11 Oct. 2011.

<sup>41</sup> see R. W. Grant and R. O. Keohane, 'Accountability and Abuses of Power in World Politics'

irrespective of the member in question. The network will, however, deal with new topics that have not been covered by binding law in any of the jurisdictions, and hence creates prospective harmonization. This, for example, is taking place in ICH's "gene therapy" working group.

Second, the topic must be domestically "implementable".<sup>42</sup> This factor is closely related to the first factor, since as long as harmonization is taking place through legally non-binding domestic guidance, there are lesser domestic procedural hurdles to overcome, and the standard becomes more easily implementable. But this factor goes further, as one can imagine that politically contentious topics that could raise serious opposition by domestic stakeholders would prevent regulators from dealing with a topic as it would not be "implementable".

These domestic preconditions are stronger than the shared ideas and understandings of the network members: Even if the network members could easily reach a consensus among themselves on a certain topic, as long as it does not pass the above preconditions, it is dropped. This suggests an important qualification to the frequent fears raised in the literature that these networks, being "epistemic communities"<sup>43</sup> of technical regulators will easily, based on their shared knowledge and interests, reach a consensus that is beyond domestic control.

Third, highly contentious topics, in which consensus would be difficult to reach are not dealt with either.<sup>44</sup> The result of this limitation is that in essence, only topics that are relatively common between the members will be discussed and harmonized. Moreover, in areas where agreement can't be reached, the language of the guideline will be vague and leaves the domestic regulators freedom of implementation, and in some cases will explicitly set out the different requirements for each of the three regions. The scope of topics that may be harmonized is, hence, limited by communality of topics.

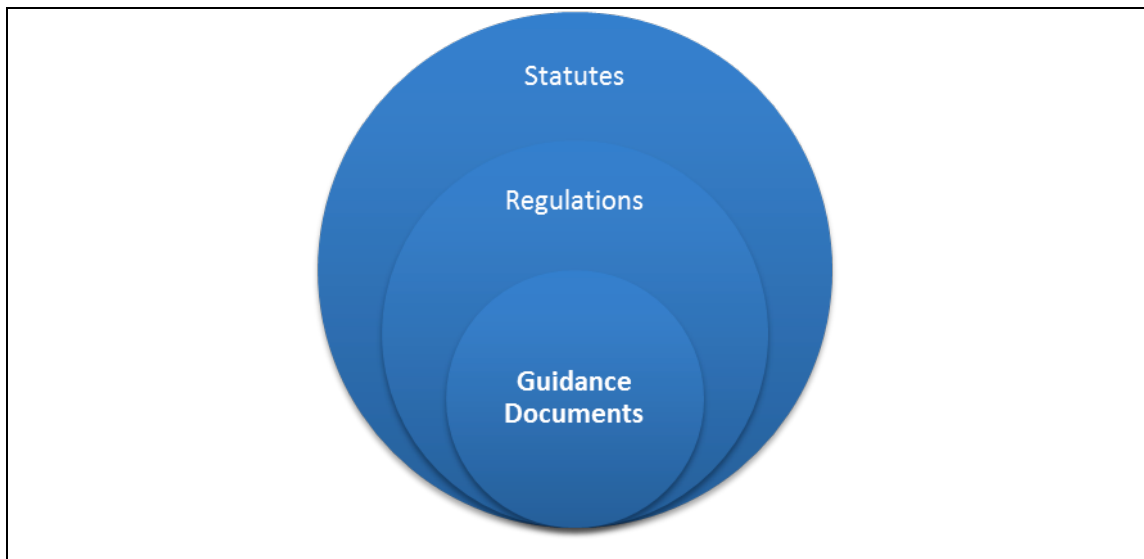
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<sup>42</sup> 'FDA ICH Public Meeting ' (20 April 2005) <http://www.regulations.gov/#!documentDetail;D=FDA-2005-N-0022-0001> accessed 11.Oct. 2011.

<sup>43</sup> Peter M. Haas, 'Introduction: Epistemic Communities and International Policy Coordination' (1992) 46 *International Organization* 1, Haas defines an epistemic community as a "network of professionals with recognized expertise and competence in a particular domain and an authoritative claim to policy relevant knowledge within that domain or issue area."

<sup>44</sup> 'FDA ICH Public Meeting' (21 January 2003) <http://www.regulations.gov/#!documentDetail;D=FDA-2002-N-0462-0002>; 'FDA ICH Public Meeting ' (20 April 2005) accessed on 11 Oct. 2011.





*[Graphic: The TRN only harmonizes topics that can be domestically implemented as legally non-binding guidance documents.]*

In light of the above, it can be concluded that topic selection is quite limited by domestic administrative practice (these limitations are not set out in any law).<sup>45</sup> This limitation suggests a serious caveat to Slaughter’s vision of “a new world order” based on transgovernmental relations, since the range of topics they can deal with, is limited.

Moreover, while these domestic restrictions limit the range of topics subject to harmonization, their counterinfluence is that they actually speed up the harmonization process and make it more efficient: By limiting themselves to topics that do not require burdensome domestic implementation procedures, harmonization takes less time. And with less cumbersome domestic implementation procedures, regulators are able to reduce fears among their transnational counterparts of domestic involuntary defection and enhance their ability to “deliver” (that is, domestically implement). This, in turn, increases the credibility of their commitments at the transnational level,<sup>46</sup> and the effectiveness of the harmonization process.

Finally, what about the counter-direction, that is, the effect of transnational topic selection on domestic interests? Putnam has made the point that negotiators may seek transnational commitments that will enable them to adopt domestically what they wish for, but are powerless to do so domestically.<sup>47</sup> That was indeed one of the main motivations for Switzerland’s Federal Banking Commission to

<sup>45</sup> That is not to say that the content of guidance documents lacks significance. These guidance documents interpret what “safe, effective and good quality” drugs means and how drugs need to be developed and tested in order to satisfy these requirements. Accordingly, they have serious and costly effects for the industry, animals and patients.

<sup>46</sup> R. D. Putnam, 'Diplomacy and Domestic Politics: The Logic of Two Level Games' 439.

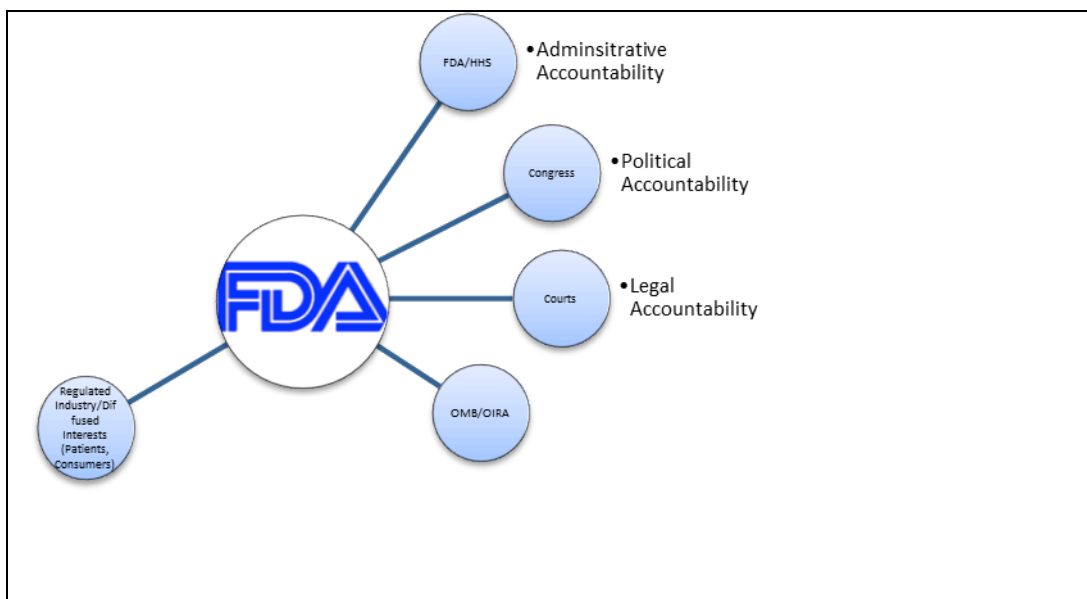
<sup>47</sup> Ibid. 457.

become a member of the Basel Committee on Banking Supervision, as they considered that if their approach would be adopted transnationally, it would be easier for them to push an international standard through parliament (as it required an amendment of Swiss law). In the harmonization networks at the center of this paper, this is not as much the case as most guidelines are adopted as guidance documents and hence do not require the approval of many “veto players” for the implementation of the guideline.<sup>48</sup>

In the following section we explore the accountability measures available to internal stakeholders towards the FDA, and the consequence thereof, in turn, for the network as a whole.

### 5. Domestic Administrative Law and Internal Accountability

Regulatory authorities, in this case the FDA, have multiple internal stakeholders: the FDA leadership, the government (mainly, the Department of Health and Human Services, Congress, OMB and the courts), the regulated (pharmaceutical) companies, and the public whose interests in the safety, quality and efficacy of drugs the FDA must protect.



*[Graphic: FDA Internal Stakeholders]*

In this section the paper considers how domestic law regulates the accountability of the FDA towards its internal stakeholders, and how this effects the network as a whole.

<sup>48</sup> A ‘veto player’ is an individual or collective actor who has to agree for the legislative [status quo](#) to change. See G. Tsebelis, *Veto Players: How Political Institutions Work* (Princeton University Press, Princeton 2002).

### ***a. The Domestic Legal Framework for Transgovernmental Harmonization***

The FDA has made international alignment and harmonization of standards a high priority.<sup>49</sup> Since 1997, with the enactment of the FDA Modernization Act, it is part of its formal mandate. Section 903(3) of the Federal Food Drug & Cosmetic Act determines that it is among the FDA's mission to "participate through appropriate processes with *representatives of other countries* to reduce the burden of regulation, *harmonize regulatory requirements*, and achieve appropriate reciprocal arrangements." Section 903(4) further encourages that this mission be carried out with private parties, that is "in *cooperation* with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products." This authority is referred to in other provisions too.<sup>50</sup>

Congress has, hence, authorized the FDA's participation in public or public-private harmonization activities. The FDA leadership has consequently also embraced this principle, and encourages the participation of FDA employees/centers in such activities in the series of FDA specific rules mentioned above.

In Section 4 we explored the ways in which these rules set procedural requirements for the network at the transnational level. But these rules also condition the participation of the FDA in transnational harmonization activities on the fulfillment of certain *domestic procedural* requirements. The Policy, for example, determines that the "... FDA's input into international standard-setting activities should be open to public scrutiny and should provide the opportunity for the consideration of views of all parties concerned".

More generally, the legal situation as regards public input into harmonization activities is fragmented in the US. While other agencies, such as the National Highway Traffic Safety Administration, EPA, or the Federal Aviation Administration (to name just some examples),<sup>51</sup> have also been obtaining citizen input regarding harmonization activity, so far there has not been issued a government-wide rule that specifically requires all agencies harmonizing domestic and foreign regulations, or that are cooperating with foreign regulators to ensure *domestic* public participation. Bodies such as the American Bar Association,<sup>52</sup> or the Administrative Conference<sup>53</sup> have made recommendations on the subject of

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<sup>49</sup> For a detailed description of the background that led the FDA to embrace international harmonization, see Ayelet Berman, 'The Public Private Nature of Harmonization Networks' (Informal International Law Making Workshop, NIAS, the Hague, Netherlands 2011 ) <[http://graduateinstitute.ch/ctei/home/working\\_papers.html](http://graduateinstitute.ch/ctei/home/working_papers.html)>.

<sup>50</sup> For example, Sec. 803(3) of the Federal Food, Drug & Cosmetic Act.

<sup>51</sup> For further examples, see R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 733-735.

<sup>52</sup> American Bar Association Section of Administrative Law and Regulatory Practice and Section of International Law and Practice Government and Public Sector Lawyers Division, 'Recommendation with Respect to Significant agency Efforts to Harmonize Domestic and Foreign Regulations through International Negotiations that may Require New Regulations or the Amendment of existing Regulations' <http://www.americanbar.org/content/dam/aba/migrated/adminlaw/harmonization.authcheckdam.pdf> accessed 11 Oct. 2011.

<sup>53</sup> Administrative Conference of the United States, 'Recommendation 91-1, Federal

international regulatory cooperation/harmonization, but a general rule has not been issued so far. In its most recent report to Congress, OIRA also recommended that “regulatory cooperation should be based, to the extent feasible and appropriate, on an open exchange of information and perspectives among the U.S. government, foreign governments, affected domestic and foreign stakeholders in the private sector, and the public at large.”<sup>54</sup> So far, however, these recommendations have not culminated into a formal government-wide rule.

### ***b. Accountability Mechanisms under Domestic Law***

As we have seen above, the FDA has been given statutory authority to collaborate with regulators and private parties on the harmonization of standards. It has also set out certain domestic procedural requirements, which the FDA must comply with. But what accountability mechanisms, if at all, oversee these transnational activities? Slaughter was among those most notably making the case that the accountability of TRNs could be improved by strengthening domestic accountability mechanisms.

As we shall see next, rather than setting up permanent, government-wide mechanisms to oversee the transnational activities of regulators (such as called for in 1991 by the US Administrative Conference), the US attitude has largely been to rely on the same accountability mechanisms which are in place to oversee purely domestic activities. In the sections below, we focus on hierarchical, supervisory, and legal accountability mechanisms.<sup>55</sup>

## **I. Supervisory Accountability**

### ***I.1. By Congress***

Congress has various oversight mechanisms of agency actions, including hearings or informal meetings, reports or adoption of legislation. Calls for congressional oversight of transnational regulatory activities are longstanding.<sup>56</sup> In the past there had been proposals for specific reporting duties concerning international harmonization (including ICH and GHTF).<sup>57</sup> But since the inclusion of transnational harmonization/collaboration as part of its mandate in 1997, the FDA reports on its international activities in its regular annual report.

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Agency Cooperation with Foreign Government Regulators' 56 FR 33842 (24 July 1991) See also George Bermann, 'Managing Regulatory Rapprochement: Institutional and Procedural Approaches' *Regulatory Co-operation for an Interdependent World* (OECD, Paris 1994) 75.

<sup>54</sup> OIRA, 'Stimulating Smarter Regulation: OIRA 2002 Report to Congress on the Costs and Benefits of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities' (2002)

[http://www.whitehouse.gov/sites/default/files/omb/assets/omb/inforeg/2002\\_report\\_to\\_congress.pdf](http://www.whitehouse.gov/sites/default/files/omb/assets/omb/inforeg/2002_report_to_congress.pdf) accessed 11 Oct. 2011.

<sup>55</sup> see R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper )' 15-16.

<sup>56</sup> See G. Bermann, 'Managing Regulatory Rapprochement: Institutional and Procedural Approaches' 89.

<sup>57</sup> 'Bill to Strengthen and Protect America in the War on Terror ', S.3 (109th Congress 1st Session 2005).

A search in the GPO database revealed that the ICH has never been the subject of any critical Congressional discussion. Similarly so for the Government Accounting Office, Congress' investigative arm. In striking contrast, the implementation of the Basel Committee's capital adequacy accords, have come under immense Congressional scrutiny, reflecting that Congress may impose significant constraints on the global activities of regulators.<sup>58</sup> This difference is presumably best explained by political rather than legal factors, such as political salience, and is beyond the scope of this paper.

## ***1.2. OIRA/OMB overview***

The Office of Information and Regulatory Affairs (OIRA), which is part of the Office of Management and Budget (OMB), an agency within the Executive Office of the President, reviews draft and final "significant" regulations and guidance documents under Executive Order 12866.<sup>59</sup> "Significance" is determined by factors such as the monetary or economic effect of the rule, or whether it raises novel legal or policy issues. The question alone of whether it was a product of international or domestic deliberation is not a factor that justifies review. Nothing in the Executive Order or other memoranda indicates that guidance the source of which is global would be exempt from OMB review. Consequently, were an ICH guideline to fall within the definition of "significant", it would be subject to the same OMB review.

## **II. Hierarchical Accountability: Within the FDA and HHS**

The FDA Center for Drug Evaluation, the FDA unit that participates in the ICH, is subject to several levels of oversight within the FDA: All harmonization activities (including the ICH, but also GHTF, ICCR, Codex, PANDRH etc.) are coordinated by the "Harmonization and Multilateral Relations Office". The Harmonization office is part of the FDA's Office of International Programs (OIP). The later is located within the FDA's Office of the Commissioner, and oversees the FDA's international activities, which include, but are not limited to harmonization. The OIP's mission is, inter alia, to assure that all FDA international interactions are "consistent with the US Department of Health and Human Services public health objectives."<sup>60</sup> Within the FDA, hence, bodies that oversee the transnational activities of FDA centers and employees, have been set up.

Moreover, during the transnational negotiation sessions the FDA representatives are constantly in touch with people in the agency, consulting with them, and getting their approvals.

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<sup>58</sup> See P.-H. Verdier, 'U.S. Implementation of Basel II: Lessons for Informal International Law-Making (Draft Paper)'

<sup>59</sup> See OMB, 'Memorandum M-09-13: Guidance for Regulatory Review ' (March 4, 2009) [http://www.whitehouse.gov/sites/default/files/omb/assets/memoranda\\_fy2009/m09-13.pdf](http://www.whitehouse.gov/sites/default/files/omb/assets/memoranda_fy2009/m09-13.pdf) accessed 10. Oct 2011, clarifying continued OIRA review of significant guidance documents.

<sup>60</sup> FDA Office of International Programs, 'Mission and Vision' <http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/ucm116430.htm> accessed 18 Oct. 2011.

The FDA also continues to be subject to the Department of Health and Human Services (HHS) oversight.

### **III. Legal accountability mechanisms**

Most of the ICH guidelines are adopted as FDA “guidance documents”. Whereas “rules” are subject to judicial review, guidance documents are subject to non-judicial appeals mechanisms as set out in the FD&C Act, FDA regulations, and the FDA’s Good Guidance Practices (GGP). Section 701(h)(4) of the Food, Drug and Cosmetic Act determines that: “The Secretary shall ensure that an effective appeals mechanism is in place to address complaints that the Food and Drug Administration is not developing and using guidance documents in accordance with this subsection.” The GGP sets out the details of the appeals mechanism, that leads up to the FDA Chief Mediator and Ombudsman.<sup>61</sup> The FDA has stressed<sup>62</sup> that these procedures complement the FDA’s dispute resolution regulations on internal review of decisions,<sup>63</sup> or citizen petitions.<sup>64</sup>

As regards cases brought before courts, while US courts have voiced in the past criticism regarding the use of guidance documents, US courts have never discussed ICH guidelines.

### **IV. Conclusion**

Slaughter has called for the development of a concept of “dual function” for all national officials. That is, an assumption that their responsibilities will include both a national and a transgovernmental component, saying that they must be accountable to their national constituents for both categories of activity.<sup>65</sup> This dual function is already reality in the FDA’s case, as transnational activities are now formally part of its mandate. As regards accountability mechanisms, the US approach has been to rely on the existing ones (i.e., those that apply to purely domestic activities). The only exception appears to be within the FDA, where special offices have been set up to oversee international activities. Moreover, in practice, even though theoretically available, Congress and the courts have expressed minor interest in the ICH. To conclude, most oversight, in the ICH’s case, is in practice taking place internally, within the agency itself, and by public comments (which we address in the next section).

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<sup>61</sup> ‘Good Guidance Practices’ 21 CFR 10.115(o).

<sup>62</sup> FDA, 'Administrative Practices and Procedures; Good Guidance Practices ( Final Rule) ' 65 Federal Register 56468 (19 September 2000) ,56473.

<sup>63</sup> 21 CFR 10.75.

<sup>64</sup> 21 CFR 10.30.

<sup>65</sup> Anne-Marie Slaughter, 'Disaggregated Sovereignty: Towards the Public Accountability of Global Government Networks' (2004) 39 Government and Opposition 159, 171, A.-M. Slaughter, *A New World Order* 218.

#### *d. Other “Responsive Promoting Measures” under Domestic Law*

##### **I. FDA Administrative Procedure for Adopting and Implementing ICH Guidelines.**

The ICH guideline drafting procedure has 5 steps, and is characterized by step-wise consultation at both the transnational and domestic level.<sup>66</sup> A “Concept Paper” put forward by one of the members or observers triggers the harmonization process. An EWG drafts a first guideline, and after its approval by the SC, the guideline leaves the ICH process and becomes the subject of regulatory consultation in the three regions. After all comments are transferred to the EWG, a renewed consensus building process takes place. Once the final draft is approved by the SC, the members implement it domestically.

The FDA adopts ICH rules as legally nonbinding “guidance documents”, (and the EMA too mostly adopts them as nonbinding “guidelines”). In some areas, such as on clinical trials or GMP, after initial adoption as a guidance, they later serve as the *de facto* basis for FDA regulations (or European legislation).<sup>67</sup>

The FDA is special in that it was the first agency to adopt a regulation on “Good Guidance Practices” (GGP). It adopted this regulation<sup>68</sup> following criticism that the extended use of guidance documents circumvented the due process of the Administrative Procedure Act (APA). The GGP was developed to provide more transparency, public participation and formality in the guidance development process,<sup>69</sup> and specifies the procedures for the development of guidance documents, and applies to ICH guidance documents too.<sup>70</sup>

According to the GGP, draft ICH guidance are subject to a notice and comment procedure,<sup>71</sup> which is very similar to the rule making procedure set forth in the APA.<sup>72</sup> The US public takes advantage of these consultation opportunities.

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<sup>66</sup> [www.ich.org](http://www.ich.org).

<sup>67</sup> In some cases, what has been adopted as a guideline can eventually find its way into a regulation or statute, e.g., the ICH GCP guidance that was initially adopted as a FDA guidance but finally was *de facto* incorporated into the FDA regulation on ‘Human Subject Protection; Foreign Clinical Studies Not Conducted under an Investigational New Drug Application’ 21 CFR 312.120.

<sup>68</sup> Initially, issued as a FDA policy but later, at Congress’ instruction under the 1997 FDA Modernization Act, as a regulation. Section 405 of FDAMA also added section 701(h) to the FD&C Act and establishes certain aspects of the 1997 GGP regulation as the law.

<sup>69</sup> For an overview of the accountability problematic of guidance documents, see OIRA ‘Stimulating Smarter Regulation: OIRA 2002 Report to Congress on the Costs and Benefits of Federal Regulations and Unfunded Mandates on State, Local, and Tribal Entities’ (2002).

<sup>70</sup> 21 CFR §10.115. It should be noted that the EMA also employs similar notice and comment procedures for the adoption of ICH guidelines as EMA guidelines. European Medicines Agency, ‘Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework’ EMEA/P/24143/2004 Rev.1 corr (2009) [http://www.emea.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/10/WC500004011.pdf](http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004011.pdf). Regarding the ICH: see Section 4.1.3. of the EMA Procedure.

<sup>71</sup> 21 CFR 10.115 (g)(1)(ii)(A) and (B) and (C); See also ICH, ‘Notes on Implementation in the Three ICH Regions’ <http://www.ich.org/cache/compo/276-254-1.html>. Accessed 11 Oct. 2011.

<sup>72</sup> Todd D. Rakoff, ‘The Choice Between Formal and Informal Modes of Administrative Regulation’ (2000) 52 Administrative Law Review 159, 168-169.

For example, on the guidance document on “Nonclinical evaluation for anticancer pharmaceuticals” around 30 comments were submitted.<sup>73</sup> The overwhelming majority of comments, however, comes from the industry.

To receive further input, the FDA may also hold public meetings or workshops; or present the draft to an advisory committee.<sup>74</sup> For example, the FDA has conducted a public workshop to receive input from experts on the “ICH S2 Genetic Toxicology Issues” guidelines.

Domestic consultation not only takes place during the harmonization process, after the first draft has been issued, but also before. Any new topic is published in the FDA’s “guidance document agenda”, which is open for public input.<sup>75</sup> Before preparing a draft guidance document, the FDA can seek or accept early public input,<sup>76</sup> or conduct public meetings or workshops.<sup>77</sup> Indeed, prior to every ICH meeting the FDA issues a notice in the Federal Register,<sup>78</sup> and holds a public meeting to update the public with topics underway and give an opportunity for public input.<sup>79</sup> The transcripts of these meetings are available online.<sup>80</sup> NGOs and industry representatives have been taking advantage of these meetings and attend them. For example, the International Councils on Animal Protection, an NGO representing European, US and Asian animal protection groups, used this opportunity to express their desire to participate in the ICH SC and EWGs when animal testing guidelines are being developed and discussed.<sup>81</sup> It is worth noting that such public meetings before ICH meetings do not take place in the EC/EMA or in Japan.

After all comments are transferred to the EWG, a renewed consensus building process takes place. The regulators will exchange the domestic comments they have received in order to arrive at a single, harmonized guideline. This point is markedly different from normal national procedures for consultation on guidelines, as the interests of other countries will be taken into account. Once consensus is reached, the guideline will be adopted by the SC, and adopted as a harmonized guideline. Once adopted as final FDA guidance documents, they are published in the Federal Register, and are made available on the FDA website.

While the GGP allows for public input, it does not require reason giving on behalf of the FDA: The FDA’s notice regarding the adoption of the final guidance

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<sup>73</sup> According to the results displayed at [www.regulations.gov](http://www.regulations.gov).

<sup>74</sup> 21 CFR 10.115(g)(1)(iii)(A) and (B).

<sup>75</sup> 21 CFR 115(f)(5).

<sup>76</sup> 21 CFR 10.115(g)(1)(i).

<sup>77</sup> 21CFR 10.115(g)(1)(i).

<sup>78</sup> e.g. FDA, 'Preparation for International Conference on Harmonisation Steering Committee and Expert Working Group Meetings in Tallinn, Estonia; Regional Public Meeting' 75 FR 18848 (13 April 2010)

<sup>79</sup> e.g. FDA, 'Transcript of the FDA 24 June 2003 ICH Public Meeting' <http://www.regulations.gov/#!documentDetail;D=FDA-2003-N-0048-0006> accessed 11 Oct. 2011.

<sup>80</sup> Transcripts of public meetings from recent years may be retrieved from [www.regulations.gov](http://www.regulations.gov).

<sup>81</sup> S. Dhruvakumar, 'FDA CDER ICH Public Meeting' (20 April 2005 )



document will typically mention that comments have been considered, and in some cases refer very generally to the topics that were revised in response to the comments received. But the FDA does not actually reason why it accepted or rejected comments. The ICH's procedural rules lack a reason-giving requirement too. It is, hence, difficult for the public to derive the extent to which comments made at the domestic level have had an impact on the final guideline (except by vigorously comparing the actual comments with the final guideline).

Finally, it should be noted that the adoption of ICH guidelines as guidance documents follows an existing trend in the past two decades, in US federal agencies, including the FDA, to increasingly set purely domestic regulatory policy through guidance documents rather than binding regulations.<sup>82</sup> That is to say that the adoption of ICH guidelines as guidance rather than rules follows an existing domestic trend rather than reflecting an exception. This practice is also widespread in other countries, such as by the EMA.

#### ***e. Assessment: Domestic Administrative Law and Internal Accountability***

As mentioned above, the most frequent charge against TRNs are that they are networks of unconstrained technocrats, or “agencies on the loose”.<sup>83</sup> As such, the problem is that regulators active in transgovernmental networks are free from the political constraints and administrative legal limitations that typically apply to regulators.

The findings of this paper demonstrate that the FDA's participation in the harmonization networks is authorized under US law, and recognized as part of its mission. Subsequently, in principle, stakeholders within the US – the government, the regulated industry and diffused interests – have measures with which they can keep the FDA accountable for its transnational activities. The stakeholders have, in fact, the same accountability measures at their disposal as those that exist for participating and overseeing guidance development activities of the FDA that are purely domestic in character – a situation that Stewart refers to as “parity”.<sup>84</sup>

These limitations on the FDA influence and restrict the decisions it can take at the transnational level. Since all ICH guidelines must be reached on the basis of *consensus*, topics that are not domestically implementable are not covered by the ICH. If there is a topic the FDA will not be able to implement, and hence will not agree to, the network as a whole can't either. This, accordingly may keep the ICH's output in line with the interests of US stakeholders that have prevailed in the domestic deliberation process. The same holds true regarding all other members that enjoy similar domestic accountability measures. It can generally be concluded that in principle, where the network works by way of consensus,

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<sup>82</sup> T. D. Rakoff, 'The Choice Between Formal and Informal Modes of Administrative Regulation' 165-166.

<sup>83</sup> A.-M. Slaughter, 'Disaggregated Sovereignty: Towards the Public Accountability of Global Government Networks', 164. Sol Picciotto, 'Democratizing Globalism' in D. Drache (ed.), *The Market or the Public Domain? Global Governance and the Asymmetry of Power* (Routledge, London 2001)338.

<sup>84</sup> R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 723.

domestic accountability measures may limit the regulators (*de jure*), and in turn limit the network as a whole (*de facto*). Moreover, all of the member regulatory agencies, with their domestic processes, taken together, arguably create a significant shield against undue influence of the industry.

This conclusion should, however, be nuanced by the following factors:

First, in practice, while formal oversight mechanisms are in place, the particular ICH activities do not seem to have drawn much attention beyond the FDA, and Congress or the Courts have not substantially dealt with it. Moreover, while the commenting procedure is open to anyone interested, comments on FDA draft ICH guidance documents have largely come from the pharmaceutical industry, and very little on behalf of consumers and patients.<sup>85</sup> The point here is that while procedures are in place, for various reasons that are beyond the scope of this paper, relevant stakeholders do not sufficiently take advantage of them.

Second, while in principle domestic measures may have a limiting effect, a separate question is, how *meaningful* they are in keeping the regulatory authorities in check with the interests of the US public. The literature, most notably Stewart, has doubted the power of domestic administrative law to provide meaningful accountability when domestically implementing global norms.<sup>86</sup> A central critique concerning international harmonization has been that procedures for harmonization are far less open to public scrutiny and participation than domestic regulatory decisional processes.<sup>87</sup> Another critique has been that the effective center of decision-making gravity lies outside of the agency, which in turn depreciates the value of domestic administrative law procedural requirements.<sup>88</sup> As we have seen, the facts of this case suggest otherwise. The procedures for developing harmonized guidelines are equally open as those that apply to domestically developed guidance. Moreover, the *early* involvement of US stakeholders in the harmonization process, rather than only at the implementation stage, suggests that they participate in the effective part of the decision-making.

On the other hand, however, and this is an important caveat, this early involvement is not effective enough, as stakeholders, say patients organizations, may comment before the ICH meetings, and after a draft has been prepared, but are not at the table with the pharmaceutical industry during the EWG's sessions. And since the consultation period is relatively short, bodies that have not been involved in its drafting have a huge educational hurdle that they must overcome within a very short period.

The decision to involve stakeholders during the actual development of the guideline in the ICH's working groups, together with regulators and industry, is a decision that would have to be made at the ICH level. This clearly points to the conclusion that while domestic measures are important, and contribute to

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<sup>85</sup> Revealed by a search of [www.regulations.gov](http://www.regulations.gov).

<sup>86</sup> R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 723.

<sup>87</sup> Ibid. 714.

<sup>88</sup> Ibid. 719.

accountability, they are not enough. In order to be more accountable, accountability measures at the global level (for example, that would allow for such involvement in the EWG) would be necessary. It is, hence a *combination* of both domestic and global procedures that will bring about better accountability. Domestic and global administrative requirements should, accordingly, be regarded as complementary in achieving internal accountability.<sup>89</sup>

Third, the fact that the FDA relies on guidance development procedures (rather than APA procedures) suggests that the accountability problem is enhanced. Whether these procedures and non-judicial appeals mechanism provide sufficient accountability is open to debate. Without the threat of judicial review, can comments on behalf of diffused social interests, such as by patients, have a limiting quality when regulators are confronted with the industry's views at the global level? While rapidly changing science justifies the use of flexible over rigid instruments, why this should be exempt from judicial review is not clear. Moreover, lacking any obligation on behalf of the regulators to reason their decision, there is no way to ensure that the consultation reflects more than mere window-dressing. .

But even were the APA to apply, domestic procedures allow for *non-voting* participation of the public, whereas industry enjoys *voting-like* participation at the transnational level,<sup>90</sup> resulting in unequal representation of interests in the decision-making at the global level. Can regulators be trusted in such an unbalanced situation not to be captured by the industry's view, and to decide on the appropriate tradeoff between maximum achievement of national social interests (such as concerning the appropriate level of standards or level of protection) and maximum regulatory alignment?

Forth, looking beyond the specific case at hand, how strong domestic administrative law may strengthen accountability depends on the specific kind of regulatory authority involved (different regulatory authorities benefit from different levels of autonomy/ accountability, think for instance of central banks that enjoy high levels of autonomy), the country the regulator originates from (different countries have different approaches as to the extent of autonomy/accountability of their regulatory authorities; and developing countries have lesser developed domestic regulatory systems),<sup>91</sup> and the procedural

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<sup>89</sup> See for a similar view, *ibid.* 754.

<sup>90</sup> Distinction between voting and non-voting participation: see R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper )' 28.

<sup>91</sup> See OECD, *Government at a Glance: 2011* (OECD Publishing, Paris 2011). See also Mark David Agrast, Boteros Juan Carlos, and Alejandro Ponce, 'The World Justice Project: Rule of Law Index' (2011) [http://worldjusticeproject.org/sites/default/files/wjproli2011\\_0.pdf](http://worldjusticeproject.org/sites/default/files/wjproli2011_0.pdf) accessed 11 Oct 2011. These reports both compare, inter alia, the levels of open and accountable government, such as transparency and participation in administrative rule making or regulatory oversight, among different countries. The indicators visually demonstrate the different levels of due process in administrative rule making among the countries. While the OECD report focuses on OECD members, the WJPRL Index is much broader and compares developed, emerging and developing countries.

requirements for implementing transnational standards (for instance implementation as guidance documents rather than as regulations). Higher levels of autonomy increase the odds of uncontrolled transnational negotiations and vice versa. It is also reasonable to expect that domestic administrative law in high-income countries with developed regulatory systems, such as in the EU, will be a serious source of accountability in comparison to developing countries with lesser developed domestic regulatory systems. But even among developed high-income countries we see variations. For example, while the FDA conducts public meetings before ICH meetings, EMA does not. Or, Swissmedic, the Swiss drug regulatory authority, adopts ICH guidelines without conducting any domestic consultations beforehand.

To conclude, the ability of domestic administrative law to control regulators (and in turn the network), has its limitations. What international lawyers should not oversee, however, is that this problem is not new, but rather a central problem inherent in the role of regulatory authorities within democratic countries.<sup>92</sup> It is a central idea in most democracies that regulators should enjoy a certain level of independence, that is, that the regulatory authority has some degree of separation from day to day political pressures.<sup>93</sup> The underlying rationale is to get technological tasks out of politics, and to insulate the civil service from partisan, electoral concerns that lead to corrupt government.<sup>94</sup> This independence gives regulatory authorities a large discretion component. Within any democratic state, regulatory authorities lack a firm democratic legitimacy basis as they are not elected, and so problems of accountability, when policy is made at the greatest remove from political controls, are already rooted in the domestic administrative system.<sup>95</sup>

The question we should be asking ourselves is, accordingly, not whether an accountability deficit exists when regulators develop guidelines— since such a deficit is given — but whether it is worsened by the transnational activities of the regulators, and what role domestic administrative law has/should have in settling the transnational-specific problems.

This then brings us to the question whether the particular characteristics of transnational activities/harmonization (being more removed than domestic processes,<sup>96</sup> the need to consider interests of foreigners and industry etc.) justify additional or specific domestic accountability measures beyond the existing ones,

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<sup>92</sup> See R.B. Stewart, 'The Reformation of American Administrative Law' (1975) 88 *Harvard Law Review* 1667, , Jerry L. Mashaw, 'Structuring a "Dense Complexity": Accountability and the Project of Administrative Law' *Issues in Legal Scholarship* (2005) <http://www.bepress.com/ils/iss6/art4>, accessed 11 Oct. 2011.

<sup>93</sup> Susan Rose-Ackerman and P. Lindseth, 'Introduction ' in S. Rose-Ackerman and P. Lindseth (eds.), *Comparative Administrative Law* (Edward Elgar Cheltenham, UK 2010) 6.

<sup>94</sup> On the rationale for regulatory independence see for example, *ibid.* 7 and Martin Shapiro, 'A Comparison of US and European Independent Agencies' in S. Rose-Ackerman and P. Lindseth (eds.), *Comparative Administrative Law* (Edward Elgar Cheltenham, UK 2010) 294, 298, 301.

<sup>95</sup> On the lack of traditional democratic accountability, see for example Susan Rose-Ackerman and P. Lindseth, 'Introduction ' *ibid.* (2010) 7.

<sup>96</sup> R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 728.

or what Stewart refers to as “parity plus”?<sup>97</sup>

On the one hand, it is questionable whether one should control regulatory authorities in their transgovernmental activities by a more stringent set of controls than what applies to their domestic activities since increased domestic control will come at the cost of the transnational bargaining, and will reduce the effectiveness of the harmonization process. Collaboration with other regulatory authorities (and private actors) has many advantages in terms of information exchange, leverage of limited resources and productivity that could not as well be achieved if each regulator were to act independently. Moreover, we live in a global economy, and the regulations made in one region of the world can have a profound effect on the development and manufacturing of our products. Consistency of approach has the possibility of eliminating redundant processes and speeds up access to markets and makes products more readily available. Thus, we should be mindful of the advantages of effective harmonization before adding more accountability measures.

On the other hand, transnational collaboration adds to the equation of regulators’ discretion additional elements that were previously not as profound, in particular the consideration of foreign and industry interests. Thus, in their transnational activities regulators should be required, within their discretion, to reasonably balance between two conflicting interests: the advantages of harmonization and the protection of the public interest. To this end, more or better domestic accountability measures should be developed.

Whatever stand one takes, and even if one were to take the stand that increased oversight is warranted, in practice, as we have seen, there does not seem to be much concern in the US government. In other countries the approach seems to be slightly different. In Canada, for example, special requirements apply to the regulators’ transgovernmental activities. There, the *Guidelines on International Regulatory Obligations and Cooperation* issued by Canada’s Treasury Board<sup>98</sup> support international regulatory cooperation, but at the same time expressly acknowledge the concerns that international alignment of regulation raises, such as the lowering of standards or of the national levels of protection. The Canadian guideline says that international obligations and international regulatory cooperation must be “achieved in ways that maintain public confidence in the Canadian regulatory system”,<sup>99</sup> and that “as such, analysis supporting regulations that pursue greater compatibility and that aim to meet other international regulatory obligations and cooperation objectives should clearly demonstrate to decision makers the benefits, costs and risks of these approaches.”<sup>100</sup> It also requires Canadian regulators to “engage stakeholders when developing international obligations and international regulatory cooperation approaches and

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<sup>97</sup> Ibid.723,728.

<sup>98</sup> Canada Treasury Board, 'Guidelines on International Regulatory Obligations and Cooperation issued by Canada’s Treasury Board' <http://www.tbs-sct.gc.ca/ri-qr/documents/gl-ld/iroc-cori/iroc-cori01-eng.asp> accessed 11 Oct. 2011.

<sup>99</sup> Ibid. Section 2.1.

<sup>100</sup> Ibid. Section 2.1.

explain to interested and affected parties why cooperating with other governments or adopting international standards benefit Canadians.”<sup>101</sup>

Finally, in keeping the role of domestic administrative law in perspective, we should not forget that domestic non-legal factors may have much greater effects on accountability -- irrespective of the legal procedures in place. This is nicely reflected if we compare the US implementation of the Basel Committee’s capital adequacy accords with its implementation of ICH guidelines. While both are networks of regulators and both had similar implementation requirements that do not formally require Congress approval (Basel to be implemented as a regulation and ICH as a guidance), Basel underwent intense Congress scrutiny.<sup>102</sup> This oversight is presumably best explained by the political salience of the topics,<sup>103</sup> the role of lobbying groups and so forth – political and economic topics that go well beyond administrative procedures.

In the following section we explore the role of domestic law for external accountability.

## **6. Domestic Administrative Law and External Stakeholders**

### ***a. Defining the External Stakeholders***

What role does and could domestic administrative law play in the accountability of the harmonization network, or in offsetting its disregard, towards external stakeholders? As mentioned above, one of the main criticisms of the ICH is that being dominated by high-income countries and the innovative pharmaceutical industry, its work has not taken into account the effects on developing countries.. Have or could domestic administrative procedures offset the disregard towards these stakeholders? We address this question below, but begin with a short overview of the ICH’s most important external stakeholders.

### **I. Non-Member Countries that Adopt ICH guidelines**

ICH guidelines are considered *de facto* global standards and are being adopted

by many countries that are not members to the network. They are also followed by producers in non-member countries (irrespective of whether the country has adopted them). From a business perspective the decision to follow ICH guidelines is quite straightforward: In order to gain access to the global pharmaceuticals market, which is dominated at around 90% by ICH countries, also outsiders must follow their standards. Moreover, many regulators consider that there is no reason for them to reinvent the wheel if “state of the art” guidelines have already been developed. Even countries that are not export-oriented adopt or rely on ICH

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<sup>101</sup> Ibid. Section 3.1.2.

<sup>102</sup> P.-H. Verdier, 'U.S. Implementation of Basel II: Lessons for Informal International Law-Making (Draft Paper)' .

<sup>103</sup> This problem of political salience is prevalent in all agencies, and also regarding their purely domestic activities. See Martin Shapiro, 'The Problems of Independent Agencies in the United States and the European Union' (1997) 4 Journal of European Public Policy 276, 288.

guidelines. They are wary of being accused of producing substandard pharmaceuticals (and the northern industry is quick to accuse them of such), and issues of pride (having the same standards as the most advanced agencies) come into play too.

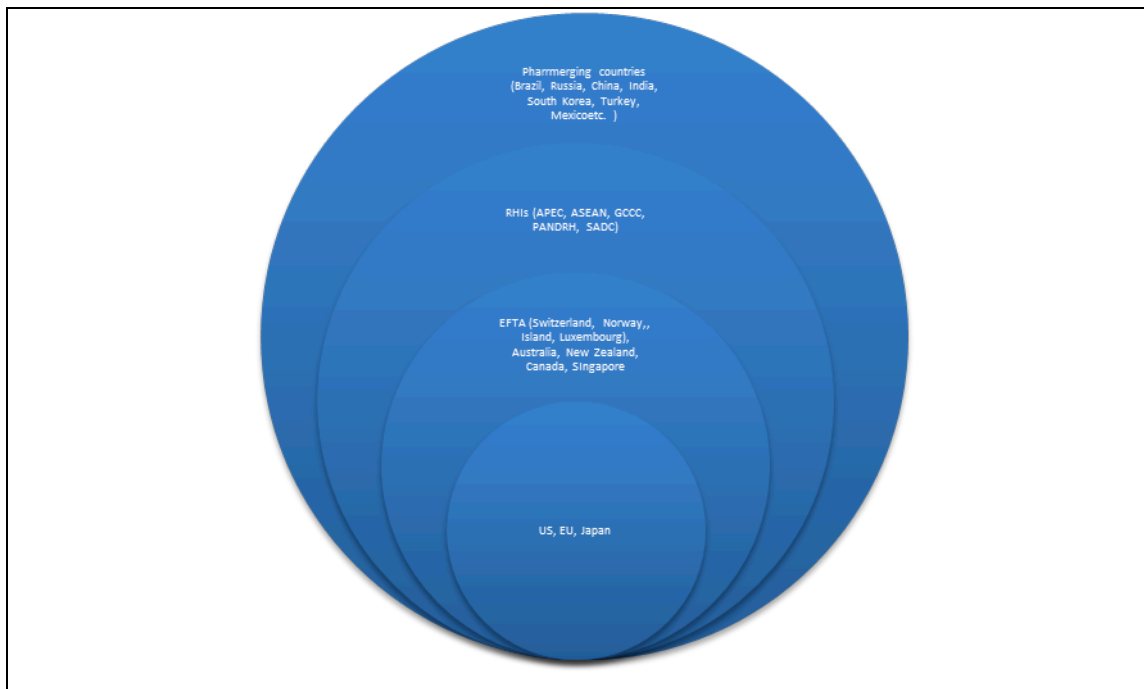
The pressure to follow ICH guidelines is not only governmental or industry driven, but also indirectly by other sectors. For example, medical journals will only publish the results of clinical trials that have been registered with a public registry, and a precondition for registration is that the clinical trial follow the ICH guideline on clinical trials.<sup>104</sup> The ICH, on its part, has also been actively encouraging the dissemination of its guidelines to non-ICH countries by setting up a “Global Cooperation Group”, providing training sessions and the like.

Within the non-member countries (and producers in non-member countries) we can distinguish roughly between three main groups:

- (i) Developed countries, such as Switzerland, Canada or Australia. The pharmaceutical industry of these countries has traditionally been dependent and linked with that of ICH members. These countries and their industries have, hence, traditionally adopted or relied on ICH guidelines.
- (ii) With the shift of pharmaceutical production to so-called “pharmerging” countries, countries such as China, Brazil, Russia and India and their industries have been following ICH guidelines too.
- (iii) Regional harmonization Initiatives (RHIs) in APEC, ASEAN, GCC, PANDRH and SADC. Their members, which include the above two groups as well as developing countries, have been adopting ICH guidelines too.

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<sup>104</sup> T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1554.



[Graphic: Growing range of countries adopting ICH guidelines.]

## II. The Problem regarding Developing Countries

The fact that non-member developing countries and their industries follow ICH guidelines raises two main concerns.

First, while ICH guidelines were initially intended for *new* drugs, quality-related guidelines are now also regularly used for *generic* drugs. ICH guidelines, accordingly, now also affect the generics industry (which is not a ICH member). The generics industry is particularly important for developing countries since most drug-production taking place there is of generics. Moreover, the main health concern of developing countries is the availability of essential drugs to its local population, and it relies to this end, on generic drugs. The WHO has raised the concern that ICH quality guidelines, being a product of high-income countries and technology driven (under the assumption that this technology will lead to increased safety of new drugs), are unnecessarily high in the sense that they are not necessarily justified by safety concerns. These standards raise manufacturing costs and are too costly for smaller pharmaceutical companies, and producers of generic drugs in developing countries.

The concern is that the adoption of ICH standards in developing countries may unnecessarily squeeze out local generic drug producers, with adverse effects on the availability of drugs to the local population. In many countries, essential drugs required for the prevention and treatment of locally endemic conditions are not supplied by the major multinationals, but by local producers. If they are unable to meet what may be unsubstantiated quality standards, the adverse impact of the withdrawal of these drugs on the health of the population would be far more dramatic than that of any hypothetical risk posed by failing to achieve ICH



standards.<sup>105</sup> This has led some NGOs to call for the development of “essential norms” that would set out the minimal quality standards from a public health standpoint.

Similarly, the guidelines on clinical trials were primarily written for commercially driven drug registration studies. Their content is unaffordable and unreachable in developing countries and so these guidelines have been an impediment to clinical research in developing countries, with potential adverse effects on the development of drugs for local needs.<sup>106</sup>

The problem that developing countries seeking to meet “western” standards may suffer consequential adverse effects goes beyond the ICH’s case and is relevant to other harmonization networks too. This often has to do with the fact that western standards incorporate a certain risk/benefit ratio that is inappropriate for developing countries. For example, VICH guidelines have also been said to represent an unachievable highest common denominator between developed countries that may not be relevant for developing countries.<sup>107</sup> The Basel Committee’s capital adequacy requirements have also been said to create major challenges to developing countries.<sup>108</sup>

The question, then, is what role domestic administrative law could or should have in solving this problem.

#### ***b. Accountability Measures at the Transnational Level***

The ICH has set up several “outreach” bodies that allow for communication with non-member countries, such as the Global Cooperation Group (bringing together the RHIs and drug regulatory authorities from “pharmerging” countries) or the Regulators Forum (bringing together regulators from pharmerging countries). The ICH has also welcomed them as non-voting participants in EWGs. The IGPA, an association of generic medicines manufacturers from the EU, Canada, US, Japan and India, has also been accepted as an “interested party”, and participates in expert working groups of relevance to its work.<sup>109</sup> Developed countries such as EFTA members, Switzerland and Health Canada have been

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<sup>105</sup> WHO, 'Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries' 2, 21-24. See also Prescire, 'ICH: An Exclusive Club of Drug Regulatory Agencies and Drug Companies Imposing its Rules on the Rest of the World' and WHO, 'Global Harmonization and the ICH'. 9.

<sup>106</sup> T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1554.

<sup>107</sup> David Mackay, 'Conclusions of the VICH 4 Conference' (VICH 4th Conference, OIE Paris 2010) <[www.vichsec.org/en/8.%20Mackay%20conclusions.ppt](http://www.vichsec.org/en/8.%20Mackay%20conclusions.ppt)>

<sup>108</sup> S. Griffith-Jones and S. Spratt, 'Will the Proposed New Basel Capital Accord have a Net Negative Effect on Developing Countries?' (2001) <https://www.bis.org/bcbs/ca/inofdest.pdf>, accessed

<sup>109</sup> e.g. Expert working group on ‘Development and Manufacture of Drug Substances : Q11’ ([www.ich.org](http://www.ich.org)) . See ICH, 'Final Concept Paper Q11: Development and Manufacture of Drug Substances' (11 April 2008) [http://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Quality/Q11/Concept\\_Paper/Q11\\_Concept\\_Paper.pdf](http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q11/Concept_Paper/Q11_Concept_Paper.pdf) accessed 11 October 2011.

observers since the ICH was first set up. The WHO is an observer too, and it is tasked with bringing the interests of those countries that are not ICH members to the table. At the ICH level, hence, we see that accountability-promoting measures exist and are continuously being introduced.<sup>110</sup>

But what does or should domestic law offer to improve the problem of disregard? One of the main criticisms against the use of domestic accountability measures for strengthening the accountability of networks has been that this would not be able to solve the problem of the disregard of the interests of non-member countries.<sup>111</sup> Is that indeed the case?

### *c. Domestic Administrative Law in Member States*

Notice and comment procedures in US rule making or guidance development are open towards “all affected parties outside of FDA”,<sup>112</sup> including foreigners.<sup>113</sup> Hence, foreign governments, companies or individuals (from any ICH non-member or member state), say from Brazil or Japan, could comment to the FDA during the ICH guideline development process. Foreigners would also have the legal or semi-legal accountability mechanisms (described above) at their disposal. The FDA has explicitly said that the notice and comment and the public meetings before ICH meetings are a conduit for input by non-ICH organizations into the ICH process.<sup>114</sup> The use of domestic procedures may, hence, be a tool for external stakeholders to voice concerns.

We see this approach of openness towards foreign stakeholders within the domestic administrative systems in many OECD countries. The EU, for example, has also taken this approach and has improved the transparency and participation of its rule making processes to foreigners.<sup>115</sup> In fact, this approach is part of the regulatory reform many OECD and APEC countries are undergoing in the past decade. The “APEC–OECD Integrated Checklist for Regulatory Reform” (2005), a checklist of regulatory reform principles for the development of good regulatory governance principles, reflecting regulatory reform principles developed since the 1990’s in a series of OECD and APEC documents, requires that the development of rules, including non-binding guidelines, be transparent and *accessible to foreign parties*,<sup>116</sup> allowing them to comment,<sup>117</sup> including their access to appeal

<sup>110</sup> See [www.ich.org](http://www.ich.org).

<sup>111</sup> See R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper)' 38.

<sup>112</sup> 21 CFR 10.115 (c)(3).

<sup>113</sup> OECD, *Regulatory Reform in the United States: Enhancing Market Openness through Regulatory Reform* (OECD Publishing, Paris 1999) <http://www.oecd.org/dataoecd/23/46/2756360.pdf> accessed 11 October 2011, p.6, 10.

<sup>114</sup> 'FDA ICH Public Meeting' (20 October 2005) <http://www.regulations.gov/#!documentDetail;D=FDA-2005-N-0395-0002>.

<sup>115</sup> American Bar Association: Section of Administrative Law and Regulatory Practice, 'European Union Administrative Law Project: About the European Union Administrative Law Project', [http://www.americanbar.org/groups/administrative\\_law/initiatives\\_awards/european\\_union\\_administrative\\_law\\_project.html](http://www.americanbar.org/groups/administrative_law/initiatives_awards/european_union_administrative_law_project.html) accessed 11 Oct. 2011.

<sup>116</sup> Principle A6 of the OECD/APEC, 'OECD-APEC Integrated Checklist for Regulatory

systems.<sup>118</sup> In May 2011 the OECD issued a “Draft Recommendation on Regulatory Policy and Governance” which recommends that regulators should “Ensure that regulatory measures contemplated in all fields take into account any international frameworks for cooperation in the same field and are also *designed to take into account their possible effects on parties outside the jurisdiction* where they are to be applied. Consultation should include any external interests with the aim of avoiding unnecessary international frictions.”<sup>119</sup>

Moreover, agreements to this end have been concluded between countries such as the US and the EU,<sup>120</sup> or US, Mexico and Canada.<sup>121</sup> And indeed, we find, for example, rules on consultation with foreign regulatory authorities in EMA’s Guideline Development Procedures,<sup>122</sup> and in Canada.<sup>123</sup>



To conclude, domestic law in the US makes certain “other responsiveness promoting measures”, and possibly a legal mechanism, available to external stakeholders. While direct participation in the network would be more ideal, in its absence, domestic procedures remain an avenue for seeking influence. Foreign entities have indeed made use of this opportunity, even if not overwhelmingly. For example, the Latin American Forum for Ethics Committees for Health Research (FLACEIS), which represents recipient countries of US companies and clinical research, submitted to the FDA comments regarding ICH guidelines on clinical trials.<sup>124</sup> Another example is the Association of the British Pharmaceutical

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Reform' <http://www.oecd.org/dataoecd/41/9/34989455.pdf> accessed 11 Oct. 2011.

<sup>117</sup> Ibid. principle D5.

<sup>118</sup> Ibid. principle A11.

<sup>119</sup> Section 12 of the OECD, 'Draft Recommendation on Regulatory Policy and Governance' (2011) <http://www.oecd.org/dataoecd/49/43/48087250.pdf> accessed 11 Oct. 2011.

<sup>120</sup> s. 4, 17 Transatlantic Economic Partnership, 'Guidelines on Regulatory Cooperation and Transparency' (2002) [http://ec.europa.eu/enterprise/policies/international/files/guidelines3\\_en.pdf](http://ec.europa.eu/enterprise/policies/international/files/guidelines3_en.pdf).

<sup>121</sup> 'Canada/United States/Mexico Security and Prosperity Regulatory Cooperation Framework'

<sup>122</sup> s. 4.7 European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework.

<sup>123</sup> s. 4 Treasury Board of Canada, 'Guidelines for Effective Regulatory Consultations'.

<sup>124</sup> Latin American Forum for Ethics Committees for Health Research (FLACEIS),

Industry, which commented to the FDA concerning a ICH genotoxicity guideline.<sup>125</sup> Lacking direct participation possibilities at the transnational level, transnational groups such as the International Council on Animal Protection, have relied on this avenue too and submit their comments on ICH guidelines directly to the FDA, the EMA and the JPMDA. Domestic procedures are also a manner for the FDA to communicate with foreigners: In the case of the GHTF, the FDA has explicitly used its notice giving procedures so as to make information about the GHTF known to developing countries.

#### ***d. Domestic Administrative Law in Non-Member States***

It is this paper's view that domestic administrative law within non-member states may have a role in compensating for the problem of disregard taking place at the global level. This is the case in the ICH, but also more generally concerning any other harmonization network.

Domestic administrative procedures may serve here in two functions. First, they generate public input in non-member countries. Thanks to ICH procedural rules that allow comments by non-members, this input may be presented to the ICH's expert working group and possibly taken into account. Second, domestic administrative procedures can allow countries to balance their domestic needs and preferences, with their interest in adopting ICH guidelines. Here domestic administrative procedures serve as a tool for tailoring the transnational standard to the national context.

It is important to note that in both cases, domestic administrative law does not function as an accountability measure, as it does not have any relationship-supporting role between the non-members and the network. Further, because they are not members and their consent is not required for the consensus, their domestic administrative limitations don't have the *de facto* power limiting power that members' domestic measures may have (as discussed above), though clearly it will often be in the network's interest to take their considerations into account (a weak accountability measures nevertheless?).

Anyway, many non-member countries are indeed relying on domestic administrative procedures in these two functions: In many developed non-member countries such as in Canada and Australia, there are domestic administrative procedures (notice and comment, publication obligations etc.) in place that allow for public input during the harmonization process, and before adoption.<sup>126</sup> China's

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'Comment on FDA Proposed Rule: Human Subject Protection; Foreign Clinical Studies Not Conducted Under an Investigational New Drug Application' <http://www.regulations.gov/#!documentDetail;D=FDA-2004-N-0061-0040> accessed 11 October 2011.

<sup>125</sup> Association of the British Pharmaceutical Industry, 'Comment on Draft Guidance on S2(R1) Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use' <http://www.regulations.gov/#!documentDetail;D=FDA-2008-D-0178-0012> accessed 11 October 2011.

<sup>126</sup> Dr Leonie Hunt, 'Use of ICH Guidelines in Prescription Medicine Regulation in Australia' (ICH Global Cooperation Group Meeting, Brussels 2008) <[http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/C-](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/C-)

State Food and Drug Administration, an emerging administration, has set up a “ICH research guideline group”, whose goal is to study ICH guidelines, compare them with Chinese guidelines, and adapt the latter while maintaining local needs.<sup>127</sup> Often non-members will rely on ICH guidelines as a source of information. The Brazilian drug regulatory authority ANVISA, for example, relies in the development of its guidelines on different international and foreign sources, including ICH guidelines.

The local adaptation of transnational standards is a phenomena prevalent in other harmonization networks too. Brazil, for example, adds higher capital adequacy requirements than those prescribed by the Basel Committee. Local adaptation makes sense: Countries vary greatly from each other in their capacities, infrastructure and preferences. A one size fits all rarely works and global standards will often need to undergo domestic adaptation, if not *de jure*, than certainly *de facto*.<sup>128</sup>

Arguably, domestic procedures could have a role to play in offsetting the problem of disregard towards the needs of developing countries: If developing countries do not have the resources to attain ICH standards, and their public health needs justify a different risk/benefit ratio than the commercially/high-income countries driven ICH guidelines,<sup>129</sup> local adaptation strikes promising. In a sense they would be free riding on goods produced by resourceful countries, and would only need to invest in adapting them to their needs. Since ICH guidelines are

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GCG\_Reports/Nov\_2008\_Brussels/DRA\_Australia\_Presentation\_in\_Brussels.pdf> accessed 11 October 2011.

<sup>127</sup> Ding Jianhua, 'Introduction of ICH China Research WG' (ICH Global Cooperation Group, Estonia June 2010) <[http://www.ich.org/fileadmin/Public\\_Web\\_Site/Meetings/C-GCG\\_Reports/June\\_2010\\_Tallinn/ICH\\_China\\_Tallinn\\_2010.pdf](http://www.ich.org/fileadmin/Public_Web_Site/Meetings/C-GCG_Reports/June_2010_Tallinn/ICH_China_Tallinn_2010.pdf)> accessed 11 October 2011.

<sup>128</sup> Also within members, administrative procedures allow to adapt to local needs. For example Switzerland, a Basel Committee member, is known for the so-called “Swiss finish” that adds higher requirements to the Basel committee’s capital adequacy requirements. The banking sector is one of Switzerland’s most important sectors and it seeks to project stability, and the local adjustment supports this goal. See also Svetiev’s paper on the ICN that describes how global antitrust norms would need to be adapted to local, factual situation. Yane Svetiev, 'Beyond the Regulatory Club: Enforcement, Norm-Generation and Learning in Transnational Networks' (2012). (forthcoming)

<sup>129</sup> Vesna Koblar, 'Impact of ICH on Non-ICH countries ' (Tenth International Conference of Drug Regulatory Authorities (ICDRA), Hong Kong 2002) <<http://apps.who.int/medicinedocs/en/d/Js4923e/7.4.html#Js4923e.7.4>> accessed 11 October 2011; WHO, 'African Medicines Regulatory Harmonization Initiative (AMRHI): a WHO concept paper' (2008 ) 22 WHO Drug Information 175, 184. The relative risk/benefit assessment may be different in developing and western countries. An excellent example is the case of the first rotavirus vaccine. It was licensed by the FDA in 1998 but was later found to have a 1 in 10000 risk of intussusception in children and was therefore withdrawn from the US market in 1999. Although this risk/benefit analysis was valid for the US, where the rotavirus causes less than 60 death per year, developing countries, where rotavirus is responsible for about 5% of deaths of children under the age of five, would have a different risk/benefit ratio. However, the benefit of the vaccine to Africa could not be realized as it was withdrawn. See The George Institute for International Health: Health Policy Division, 'Registering New Drugs: The African Context: New Tools for New Times' (2010) [http://www.dndi.org/images/stories/advocacy/regulatory-report\\_george-institute-dndi\\_jan2010.pdf](http://www.dndi.org/images/stories/advocacy/regulatory-report_george-institute-dndi_jan2010.pdf) P. accessed 11 October 2011.

considered unnecessarily high (that is, not justified by safety/quality/efficacy concerns) for generic medicines or some clinical trials, by adapting the standards, local development and production of medicines, and in turn their accessibility, would not be undermined.<sup>130</sup>

That said, in practice, there are several limitations on using domestic law as a tool to offset the problem of disregard. First, the market being dominated by ICH countries, in remaining globally competitive (and to be able to sell in the big ICH market), guidelines of non-member countries may not be substantially different from ICH guidelines. Local adaptation of standards is, accordingly, not a significant option for *export* oriented countries/products (such as Canada or China), but rather concerns production for *local* needs. A second concern is that many developing countries have insufficient regulatory capacity, and poorly developed regulatory authorities, or no regulatory authority at all, making formal local adaptation unfeasible.<sup>131</sup> The third concern is that in some cases, local adaptation could lead to double standards between “western” and “third world” standards,<sup>132</sup> or between standards for export-oriented products and products for local use. This raises ethical concerns that are beyond the scope of this paper. Finally, many countries would be unwilling to adapt the standards as this could be regarded as inferior.<sup>133</sup> Hence, to enjoy legitimacy, adaptation to the needs of developing countries could be conducted with the WHO’s support. Indeed, the World Animal Health Organization is currently considering such support in the context of adaptation of VICH guidelines to local needs.

In practice, many developing countries *de facto* adapt the guidelines to their local needs. That is to say that it will often be the case that the local drug regulatory authority will have formally fully adopted the international guideline, but with the standards being too high for local producers to comply with, will not enforce them in practice. This is, for example the case in Tanzania, where local authorities formally adopt international standards, but for industrial policy purposes, support local producers by not enforcing international standards.<sup>134</sup> In India, production ranges enormously in its quality. Export-oriented drugs follow international standards and are of high quality, whereas drugs produced for local use are of lower quality. In this case too, the Indian drug authorities simply turn a blind eye regarding the latter.

This brings to the conclusion that in order to improve the network’s accountability towards its external stakeholders, the best way would be to involve

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<sup>130</sup> See also P. Kourilsky and I. Giri, 'Safety Standards: an Urgent Need for Evidence-Based Regulation' *Surveys and Perspectives Integrating Environment and Society* (2008) <http://sapiens.revues.org/219>, accessed 11 October 2011.

<sup>131</sup> T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1555.

<sup>132</sup> V. Koblar, 'Impact of ICH on Non-ICH countries '.

<sup>133</sup> T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1554.

<sup>134</sup> Chukilizo Nditonda B., 'Availability and Quality of Medicines in Low Income Countries: The Role and Opportunities for European Manufacturers' (23rd Annual DIA EuroMeeting, Geneva, Switzerland 2011).

their interests at the transnational level. In addition, a *prerequisite* to the transnational involvement of developing countries is the existence in such countries of a functioning drug regulatory authority.<sup>135</sup> Thus, we can't really talk about accountability without having proper domestic institutions in place. But regulatory capacity is low in developing countries. In Africa, for example, the overwhelming majority of African drug regulatory authorities lack capacity and resources.<sup>136</sup> Thus, efforts to improve accountability towards developing countries should be combined with assisting these countries to develop domestic regulatory capacities. For accountability to be meaningful at the transnational level, it must, hence, be bound with the notion of development. This will be the foundation that will eventually lead to greater accountability.

An alternate solution would be, as mentioned above, to let the WHO take on the responsibility of representing the interests of developing countries. To that end, the WHO would become a full member on the ICH as some NGOs have called for; or it would independently develop more sensible guidelines on the basis of ICH guidelines.

## 7. Conclusion

The purpose of this paper has been to explore the role domestic law has to play in the accountability of TRNs, in particular of harmonization networks. The paper has come to several conclusions.

First, domestic law may condition the participation of regulators in TRNs on the fulfillment of procedural or substantive requirements by the transnational networks. Where such rules are set by powerful member states, whose participation in the network is cardinal, the rules will apply *de facto* to the network as a whole. If more than one country imposes similar requirements, we can expect to see more TRNs designed in accordance with good administrative procedures. Domestic law should, hence, be reformed to this end.

Second, domestic law and practice may limit the scope of the topics negotiated at the transnational level. Our findings here suggest a serious caveat to Slaughter's vision of a new world order based on transgovernmental networks.

Third, domestic accountability measures in member countries may have an important role to play in keeping the regulators, and in turn the network as a whole, accountable towards the interests of their internal stakeholders. That is in particular the case when decisions in the network need to be reached by consensus. The extent to which domestic administrative law can keep the regulators accountable may vary. The stronger the domestic accountability measures (depending on the specific kind of regulatory authority/

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<sup>135</sup> This is understood as full drug registration processes, pharmaceutical inspection services and certified compliance with good manufacturing practice. See WHO, 'Global Harmonization and the ICH'. 9.

<sup>136</sup> DNDi Report on Africa, 6. See also WHO: Regional Committee for Africa, 'Medicines Regulatory Authorities: Current Status and the Way Forward' (2006) <http://www.afro.who.int/en/fifty-sixth-session.html> accessed 11 October 2011.

country/implementation procedures at hand), the stronger these domestic measures as a source of accountability. In thinking about the future, countries should consider strengthening or improving the domestic accountability measures that apply to the transnational activities of their regulators.

In any event, domestic measures can only restrict to a certain event. In view of achieving better accountability towards internal stakeholders, domestic measures must be complemented by accountability measures at the transnational level. Only a combination of both will allow for meaningful accountability towards internal stakeholders. And indeed, what we see today is that at both the domestic and transnational levels there is a gradual trend of increased transparency and participation.

As regards external stakeholders, domestic administrative law in the US (as well as in other countries) is opening up towards external stakeholders, and provides an additional avenue for voicing concerns.

Further, domestic law in non-member countries may allow adapting transnational standards to local needs. In this case administrative law does not serve as an accountability measure, but rather as a tool to tailor transnational standards to the local context. In practice, this approach comes across several problems. Consequently, domestic administrative law as a tool to set off disregard towards external stakeholders, while having some merit, has relatively little to offer. The interests of non-member countries, their industries or their diffused interests need to be taken into account at the transnational level. This brings my conclusion closely to that of others that have argued that domestic accountability procedures do not solve the problem of the disregard of the interests of non-member countries.<sup>137</sup>

But here too, accountability measures at the transnational level are not meaningful if a country does not have domestic regulatory capacities in place that serve as a basis for meaningful participation. Domestic regulatory capacity is a *precondition* for accountability at the transnational level (unless one accepts that “surrogates” such as intergovernmental organizations or NGOs represent the interests of those developing countries that lack the capacity to represent themselves.) Real, rather than “window-dressing” accountability at the transnational level, hence, needs to begin domestically.

To conclude, domestic law is important in improving the accountability of TRNs towards internal stakeholders, and has some role, albeit limited, in offsetting the problem of disregard towards external stakeholders. Accountability measures at the transnational level remain important too. They are important in improving the accountability towards internal stakeholders, and are critical when it comes to external stakeholders. In designing domestic or transnational accountability measures, these factors should be kept in mind.

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<sup>137</sup> See R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper)' 38.