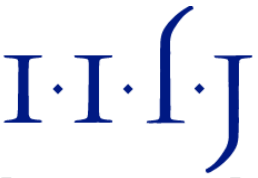

INSTITUTE FOR INTERNATIONAL LAW AND JUSTICE
NEW YORK UNIVERSITY SCHOOL OF LAW

Institute for International Law and Justice Emerging Scholars Papers

IILJ Emerging Scholars Paper 22 (2012)
(A Sub series of IILJ Working Papers)

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

Ayelet Berman

Institute for International Law and Justice:
New York University School of Law
139 MacDougal Street, 3rd Floor
New York, NY 10012
Website: www.iilj.org

ISSN: 1552-6275

New York University School of Law
New York, NY 10012
U.S.A.

Cite as:
IILJ Emerging Scholars Paper 22 (2012)
(A Sub series of IILJ Working Papers)
Finalized 02/20/2012

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

Ayelet Berman[1]

1. Introduction

Cooperation amongst regulatory authorities 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 "transgovernmental regulatory networks" ("transnational" when in collaboration with private actors)[2] (TRNs) has been concerned with their accountability deficits. TRNs have been said to lack transparency,[3] and criticized for their "club–like" nature – dominated by the U.S. and Europe while affecting third countries, particularly developing countries, which do not adequately participate in their procedures.[4] Moreover, it has been argued that affected nongovernmental actors are not sufficiently involved.[5] A related charge against TRNs has been that they are networks of unconstrained technocrats, or "agencies on the loose",[6] the main concern being the lack of domestic political or legal control over the bureaucracy,[7] and the shifting of

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Use of the FDA logo in figures is for the purpose of clarity and readability only, and is not intended to suggest that the FDA endorses or is affiliated with any aspect of this scholarly work.

[1] PhD candidate, International Law Unit, Research Assistant, Centre for Trade and Economic Integration, Graduate Institute of International and Development Studies, Geneva. The research for this paper has enjoyed partial funding by the Hague Institute for the Internationalisation of Law (HiiL). For their helpful comments I thank participants at the 7th Global Administrative Law (GAL) seminar on "Private and Public-Private Global Regulation: Global Administrative Law Dimensions" (Viterbo/Italy,10-11, June 2011), participants at the "Informal International Law Making: Domestic Elaboration and Implementation" workshop at the HiiL Law of the Future Conference, (The Hague, 23-24 June 2011), as well as Megan Donaldson at the IILJ. This paper has also benefited from interviews and discussions conducted with former and current employees of drug regulatory authorities, intergovernmental organizations and NGOs.

[2] Anne-Marie Slaughter, *A New World Order* (Princeton University Press, Princeton 2004).

[3] 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.

[4] David Zaring, 'Informal Procedure, Hard and Soft, in International Adminsitration' (2005) 5 Chicago Journal of International Law 547, 595.

[5] 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.

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

[7] Benedict Kingsbury, Nico Krisch, and Richard B. Stewart, 'The Emergence of Global Adminsitrative 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.

decision-making away from accessible, accountable national governments to international bodies that are inaccessible to citizens.[8]

While most of the accountability literature has focused on accountability measures available at the global level,[9] this paper seeks to expand the analysis by examining the role that domestic administrative law and practice (in short, domestic administrative law) might play in relation to the accountability of TRNs. In particular, the paper seeks to understand the role of domestic administrative law in the context of "harmonization networks": TRNs that are in the business of harmonizing rules or otherwise producing normative output (such as standards, guidelines, best practices, recommendations etc.)

The question of how to keep such harmonization networks accountable will become more important over time. The alignment of diverging technical or social regulations, or what has been termed "3rd generation barriers to trade,"[10] 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,[11] with many initiatives already underway (for example between the U.S. and the EU,[12] or U.S.-Canada-Mexico,[13] to name just a few.) Moreover, with globalization and the shift of supply chains to third countries, the harmonization of standards – so as to ascertain the safety and integrity of supply chains – is a central building block of the strategy of drug regulatory authorities for the 21st century.[14] Collaboration with the private sector to this end is considered important too.

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[8] 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.

[9] 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 ' in J. Pauwelyn, R. Wessel, and J. Wouters (eds.), *Informal International Lawmaking* (Oxford University Press, Oxford 2012 (forthcoming))

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

[11] 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.

[12] 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 accessed 11 Oct. 2011.

[13] '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 accessed 11 Oct. 2011.

[14] See US Food and Drug Adminsitration, 'Pathway to Global Product Safety and Quality' (2011) http://www.fda.gov/downloads/AboutFDA/CentersOffices/OC/GlobalProductPathway/UCM262528.pdf accessed 11 October 2011; and FDA, 'Strategic Priorities 2011-2015: Responding to the Public Health Challenges of the 21st Century' (2011) http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM252092.pdf accessed 11 October 2011, p. 8.

The paper outlines an analytical framework for assessing the role of domestic administrative law in the accountability of harmonization networks, and applies this framework to a case study of U.S. administrative law and the International Conference on the Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), a network of drug regulatory authorities and industry associations from the U.S., EU and Japan that harmonizes the technical requirements of drug registration rules.

While this paper focuses on U.S. law and the ICH as a case study, the analytical framework proposed, and the specific conclusions reached, can serve our analysis of harmonization networks in other fields. This paper argues that domestic law is significant in establishing the accountability of harmonization networks to internal stakeholders, and has some role to play, albeit a limited one, in addressing the problem of disregard of external stakeholders. Transnational accountability measures, on the other hand, are critical for external accountability, but also provide an important means of improving accountability to 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. Section 3 provides a short overview of the ICH. Section 4 concerns the role of domestic law in setting procedural rules for the network. Section 5 concerns the role that domestic law plays in maintaining the accountability of the FDA, and in turn the network in its entirety, to internal stakeholders. To this end, it addresses the domestic law that regulates transnational harmonization (5A), the accountability mechanisms (5B) and "other responsiveness promoting measures" provided by domestic law (5C), and summarizes findings (5D). Section 6 concerns the role that domestic law plays in the accountability of the network to external stakeholders. Following a short introduction of the main external stakeholders (6A) and the main transnational accountability measures (6B), the paper discusses the role played by domestic law in both member countries (6C) and 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" to, or conversely "disregard" of, the interests of others.[15] As regards these "others" to whom the actor should be accountable, the paper presumes a

[15] 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: Framing the Concept and Research Questions' in J. Pauwelyn, R. Wessel, and J. Wouters (eds.), *Informal International Lawmaking* (Oxford University Press, Oxford 2012 (forthcoming))

distinction between accountability to "internal" and "external" stakeholders.[16] The paper further relies on the distinction between (i) decision rules (such as rules determining who may vote), (ii) accountability mechanisms (i.e., procedures whereby specified stakeholders have the authority to demand that specified power-holders give an account of their conduct, and to 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).[17] 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 is accountability of the network to *internal stakeholders*. Internal stakeholders are those that are behind the TRN *members* (in this case, ICH members are governmental regulatory authorities and industry associations). Focusing here on the governmental members, internal stakeholders are the stakeholders that are within the TRN's member countries: within each member country we have the businesses regulated by the networks' output, and the individuals and other diffuse social interests within the member country affected by this output. Moreover, within each member country we have the governmental bodies and courts that are in charge of overseeing the regulatory authorities. To maintain analytical clarity, the paper considers all such governmental and nongovernmental stakeholders within member countries to be internal stakeholders.

The second concern in thinking about accountability of a harmonization network is the network's responsiveness to/disregard of *external stakeholders*. External stakeholders are non-member countries that adopt a network's guidelines, as well as businesses or diffuse social interests affected by the network's output and not represented by network members. External stakeholders obviously include businesses and social interests from non-member states, but potentially also, 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 examine accountability measures that exist for both internal and external stakeholders. These stakeholders are shown, for ICH, in Figure 1 overleaf.

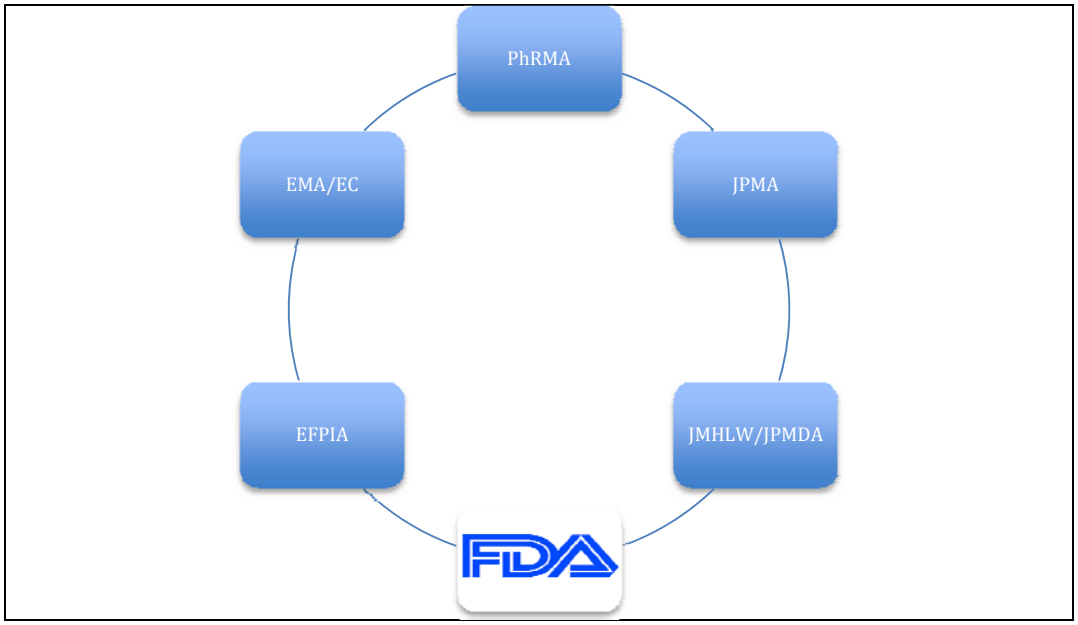
[16] Ruth W. Grant and Robert O. Keohane, 'Accountability and Abuses of Power in World Politics' (2005) 99 American Political Science Review 29, 31.
[17] J. Pauwelyn, 'Informal International Law-Making: Framing the Concept and Research Questions', R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper)' .

Figure 1. 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),[18] or we can think of it as comprised of *interconnected nodes* (in this case, of national regulatory authorities and industry associations – see Figure 2 overleaf). 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. This paper contributes to the ongoing debate on accountability by zooming in on something different, the "node", or the regulatory authority, and checking empirically the role that domestic law is playing and could play in the accountability of such regulatory authorities and, in turn, the network as a whole, to internal and external stakeholders.

[18] 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.

Figure 2. The ICH as interconnected nodes



Hence, in our analysis of accountability, it is helpful to divide the harmonization process into two levels and to examine the accountability measures (to 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 accountability (to both internal and external stakeholders) at the domestic level.

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.[19] 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 bargaining and decision-making at the international level.

[19] Robert D. Putnam, 'Diplomacy and Domestic Politics: The Logic of Two Level Games' (1988) 42 International Organization 427, 434.

This paper is very much in line with Putnam's argument and seeks to provide insights into the impact that domestic administrative law has on the accountability of the transnational bargaining process.

The idea of addressing the accountability problems of TRNs through boosting domestic accountability procedures has been advanced by Slaughter and others.[20] Since TRNs are composed of regulators, which in turn are bound by domestic administrative law, this avenue of research seems promising. While Slaughter's work focused on purely transgovernmental networks, this paper argues that domestic administrative law may be equally relevant for TRNs such as the ICH, in which regulators collaborate with private actors.

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

3. Background on the ICH

The ICH was set up two decades ago, and is composed of drug regulatory authorities and R&D pharmaceutical industry associations (i.e. industry associations representing companies engaged in the development of *new* drugs) from the U.S., EU and Japan. The governmental regulatory authority members are the U.S. Food and Drug Administration (FDA), the European Commission DG Health and Consumers, the European Medicines Agency (EMA), the Japanese Ministry of Health, Labor & Welfare (JMHLW) and the Japanese Pharmaceuticals and Medical Devices Agency (JPMDA). The industry members 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 interested parties may attend too, such as the WHO, Swissmedic (the Swiss drug regulator) on behalf of EFTA countries, Health Canada (the Canadian drug regulator), or the International Generic Pharmaceutics Alliance (IGPA) (as well as other ad hoc observers). The Secretariat is run in Geneva by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

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. The industry and regulatory authorities members enjoy an equal number of seats in the decision-making organs – the main organs being the "Steering Committee" which governs the ICH and the "expert working groups" that develop the guidelines. Decisions are reached by way of consensus among the six members.

In the Steering Committee the six founding members each have two seats. Observers and the IFPMA attend too. As of recently, certain non-ICH drug regulatory authorities (non-ICH DRA's) and regional harmonization initiatives (RHI's) have been invited to

[20] 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.

attend as well. The “expert working groups” work under the general headings of “Efficacy”, “Quality”, “Safety” and “Multidisciplinary” topics. Here too, each of the six members nominate two experts per working group, and observers and the IFPMA each nominate one expert. If appropriate, interested parties appoint one too. In 2010 the ICH officially opened the working groups to active participation by non-ICH DRA’s and RHIs experts.

The guidelines developed in the working groups are endorsed by the Steering Committee as legally non-binding guidelines, which are in most cases implemented nationally as legally non-binding rules (FDA “guidance documents”/EMA “guidelines”). In practice, many of its guidelines have become global standards adopted by a wide range of countries, including those not represented by members of the ICH. [21]

4. Domestic Administrative Law and the Transnational Level

In the U.S. it has been a long-standing approach to encourage the participation of federal agencies in standard-setting activities outside of the government (whether domestic or international, private or 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”, dating back to the 1970s. The "National Technology Transfer and Advancement Act”, passed in 1995, codifies the Circular. Following and based on the Circular and NTTAA, the FDA has 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,” [22] the “Policy on the development and use of standards with respect to international harmonization of regulatory requirements and guidelines,”[23] and the Staff Manual Guide 9100.1 “Development and Use of Standards.”[24]

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 on “Participation in outside standard-setting activities” demands that a private standard-setting activity in which

[21] For more information about the ICH see www.ich.org; see also A. Berman, ‘ Informal International Law-Making in Medical Products Regulation’ in J. Pauwelyn, R. Wessel, J. Wouters (eds.) *Informal International Law-Making: Case Studies* (TOAEP, 2012) (forthcoming); A. Berman, “Public-Private Harmonization Networks: The Case of the International Conference on Harmonization (ICH)” 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, 3rd edition, 2012) (forthcoming).
[22] 21 CFR 10.95.
[23] FDA, 'International Harmonization: Policy on Standards (Notice)' 60 Federal Register 53078 (11 October 1995) .
[24]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.

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."[25] The Policy on development and use of standards similarly determines that the activity's "development process for the standard is transparent (i.e., open to public scrutiny), complies 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".[26] The Policy also sets out *substantive* 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*."[27]

While the US acknowledges the advantages associated with governmental collaboration with private actors in standard-setting, it is equally understood that such collaboration raises concerns about regulatory capture and need to safeguard the public interest. [28] The rules discussed above were introduced so as to encourage compliance with public interest safeguards, and to bring the FDA's 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 harmonization activity from inappropriate industry influence, and guard the scientific integrity of the process. Moreover, the very fact that regulators participate was also considered a safeguard of the public interest.

It is often claimed that TRNs fall into the cracks between domestic and international law.[29] But since U.S. federal agencies may only (formally) participate in 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 impose good administrative practices on the TRN. As a result, while U.S. law does not *de jure* apply to the network, it may do so *de facto*. This is a "bottom up" approach of extending U.S. administrative law to global procedures.[30] 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

[25] 21 CFR 10.95 (d)(5).
[26] FDA 'International Harmonization: Policy on Standards (Notice)' (11 October 1995), s. IV(A)(3).
[27] Ibid. s. I(B)(1) (emphasis added)
[28] 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.
[29]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 accessed 11.Oct.2011.
[30] R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 753-754.

generally, it can be concluded that a network may be *de facto* bound by the domestic legal requirements of its most dominant participants.

In fact, good administrative practice is also often extended "bottom up" by the regulators to their transnational activities without any specific obligation set out in domestic laws, but merely as a reflection of the nature of domestic practices. For instance, at the EC's initiative, the International Cooperation on Cosmetic Regulation (ICCR)—a cosmetics harmonization network which is closely related to the ICH—recently convened an ICCR stakeholders meeting, without being under any legal obligation to do so, at which industry and NGOs voiced their views and requests.[31]

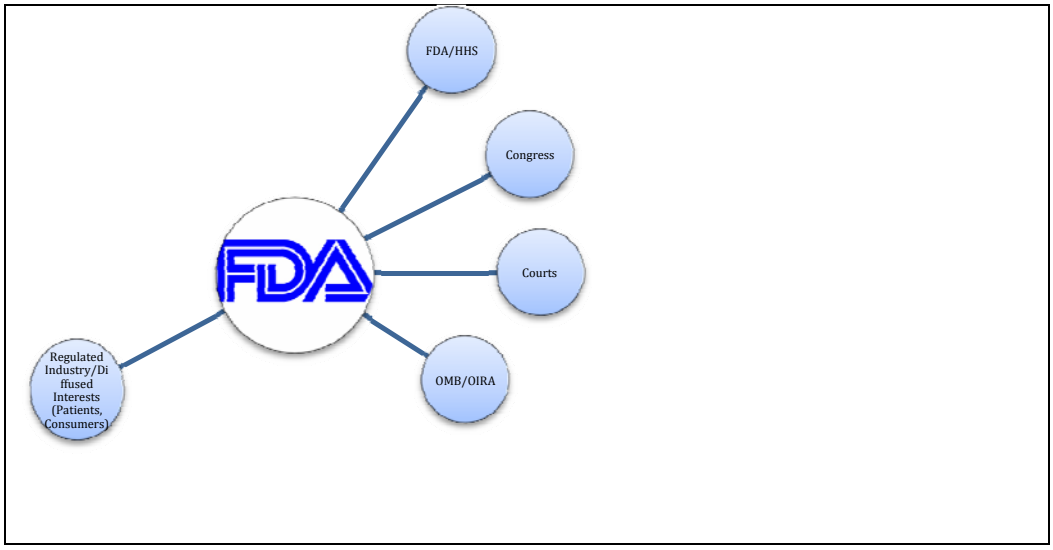
The point to take from these cases is that, even in the absence of any international agreements on such topics, "bottom up" or "extraterritorial" insistence on good administrative practice may be an efficient way to achieve the goal of ensuring good administrative practice at the transnational level. Although this bottom-up diffusion may occur even in the absence of formal rules, one way to advance this "bottom up" diffusion of good administrative practice would be for powerful international actors such as the U.S. and EU to include conditions in their laws that would *de jure* bind regulators in their transnational activities, and would in turn *de facto* bind the TRNs in which these regulators participate.

5. Domestic Administrative Law and Internal Accountability

Internal accountability may be secured by regulatory authorities, in this case the FDA, and other actors – the FDA leadership, the government (mainly, the Department of Health and Human Services, Congress, the Office of Management and Budget (OMB), the Office of Information and Regulatory Affairs (OIRA) and the courts, the regulated (pharmaceutical) companies, and the public whose interests in the safety, quality and efficacy of drugs the FDA must protect (see Figure 3 overleaf).

[31] Laurent Selles (EC Health and Consumers DG), 'Announcement of ICCR-5 Stakeholder Session in Paris, June 30, 2011' (2011) http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/iccr_june2011_en.pdf accessed 11. Oct. 2011.

Figure 3: The FDA and Mechanisms for Internal Accountability



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

A. The Domestic Legal Framework for Transgovernmental Harmonization

The FDA has made international alignment and harmonization of standards a high priority.[32] Since 1997, with the enactment of the FDA Modernization Act, this is part of its formal mandate. Section 903(3) of the Federal Food Drug & Cosmetic Act determines that it is a part of 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."[33] Section 903(4) further requires that this mission be carried out, "as determined to be appropriate by the Secretary", with private parties, namely "in *cooperation* with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products." This authority is referred to in other provisions too.[34]

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

[32] 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/webdav/site/ctei/shared/CTEI/working_papers/CTEI-2011-06.pdf>.
[33] Emphasis added.
[34] For example, Sec. 803(3) of the Federal Food, Drug &Cosmetic Act.

activities in the series of FDA specific rules mentioned above. The FDA also has a line item for ICH activity in their annual budget.

These rules set procedural requirements for the network at the transnational level, but they also make participation of the FDA in transnational harmonization activities conditional 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 U.S. While other agencies, such as the National Highway Traffic Safety Administration, EPA, or the Federal Aviation Administration (to name just some examples),[35] have also been obtaining citizen input regarding harmonization activity, so far the government has not issued a government-wide rule that specifically requires all agencies engaged in harmonizing domestic and foreign regulations, or collaborating with foreign regulators, to ensure *domestic* public participation. Bodies such as the American Bar Association[36] and the Administrative Conference[37] have made recommendations on the subject of international regulatory cooperation/harmonization, and 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."[38] So far, however, these recommendations have not culminated in 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. Domestic rules have also set out certain domestic procedural requirements with which the FDA must comply. But what accountability mechanisms, if at all, apply to collaboration in TRNs?

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[35] For further examples, see R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 733-735.

[36] 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.

[37] Administrative Conference of the United States, 'Recommendation 91-1, Federal 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.

[38] 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 accessed 11 Oct. 2011.

As we shall see next, rather than setting up permanent, government-wide mechanisms to oversee the transnational activities of regulators (as called for in 1991 by the U.S. Administrative Conference), the U.S. 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 supervisory, hierarchical and legal accountability mechanisms.[39]

1. Supervisory Accountability

a) Oversight by Congress

Congress has various mechanisms for the oversight of agency actions, including hearings or informal meetings, reports or adoption of legislation. Calls for congressional oversight of transnational regulatory activities are longstanding.[40] In the past there have been proposals for specific reporting duties concerning international harmonization (including ICH and the Global Harmonization Task Force, a network that harmonizes registration regulations applying to medical devices),[41] 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.

A search in the Government Printing Office database reveals 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, implementation of the Basel Committee's (also, a harmonization network) capital adequacy accords has come under immense Congressional scrutiny, indicating that Congress may, if it so desires, impose significant constraints on the global activities of regulators.[42] This difference between the significant attention directed to the Basel Accords, and the lack of Congressional criticism of other TRNs including the ICH is presumably best explained by factors such as their different degrees of political salience, and is beyond the scope of this paper.

b) Oversight by OIRA/OMB

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.[43] "Significance" is determined by factors such as the

[39] see R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper)' 15-16.
[40] See G. Bermann, 'Managing Regulatory Rapprochement: Institutional and Procedural Approaches' 89.
[41] 'Bill to Strengthen and Protect America in the War on Terror ', S.3 (109th Congress 1st Session 2005).
[42] See P.-H. Verdier, 'U.S. Implementation of Basel II: Lessons for Informal International Law-Making '
[43] 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 accessed 10. Oct 2011.

monetary or economic effect of the rule, or whether it raises novel legal or policy issues. The question of whether a regulation or guidance document was a product of international or domestic deliberation is not, by itself, a factor that justifies review. However, 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 as a document developed domestically.

2. 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 Alimentarius, Pan-American Network for Drug Regulatory Harmonization etc.) are coordinated by the "Harmonization and Multilateral Relations Office", which is part of the FDA's Office of International Programs (OIP). The latter 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 U.S. Department of Health and Human Services public health objectives."[44] Within the FDA there are thus several bodies that oversee the transnational activities of FDA centers and employees. The FDA also continues to be subject to oversight by the Department of Health and Human Services (HHS).

3. 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 Food, Drug and Cosmetic Act (FDCA), FDA regulations, and the FDA's Good Guidance Practices (GGP). Section 701(h)(4) of the FDCA provides 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, which involves the FDA Chief Mediator and Ombudsman.[45] The FDA has stressed[46] that these procedures complement the FDA's dispute resolution regulations on internal review of decisions,[47] and citizen petitions.[48]

As regards cases brought before courts, there has been only one instance in which a U.S. court has addressed ICH guidelines. The case, Aventis v. Lupin, concerned a

[44] FDA Office of International Programs, ' Mission and Vision' http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofGlobalRegulatoryOperationsandPolicy/OfficeofInternationalPrograms/ucm116430.htm accessed 18 Oct. 2011.
[45] 'Good Guidance Practices' 21 CFR 10.115(o).
[46] FDA, 'Administrative Practices and Procedures; Good Guidance Practcies (Final Rule) ' 65 Federal Register 56468 (19 September 2000) , 56473.
[47] 21 CFR 10.75.
[48] 21 CFR 10.30.

dispute over an alleged patent infringement. The defendant argued (among other things) that the fact that the FDA had relied on ICH guidelines in commenting on his product undermined the plaintiff's patent infringement allegations. What is interesting for our discussion is that the court found that the FDA had not adopted the ICH guideline. It reasoned that the fact that a FDA guidance document incorporated the ICH guideline does not matter, as guidance documents are not legally binding (a guidance document "does not create or confer any rights for or on any person and does not operate to bind FDA or the public"). The court was also not convinced that the FDA had endorsed the ICH guideline.[49]

4. Conclusion

Slaughter has called for the development of a concept of "dual function" for all national officials, namely 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.[50] This dual function is already a reality in the FDA's case, as transnational activities are now formally part of its mandate. As regards accountability mechanisms, the U.S. approach has been to rely on 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 as oversight mechanisms, Congress and the courts have had little to say about 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).

C. Other "Responsive Promoting Measures" under Domestic Law

The ICH guideline drafting procedure has 5 steps, and is characterized by step-wise consultation at both the transnational and domestic level.[51] A "Concept Paper" put forward by one of the members or observers triggers the harmonization process. An expert working group drafts a first guideline, and after its approval by the Steering Committee, the guideline leaves the ICH process and becomes the subject of regulatory consultation in the three regions.

As ICH guidelines are eventually adopted as FDA guidance documents, at this domestic consultation stage, the ICH guidelines are subject to the FDA's regulation on "Good Guidance Practices" (GGP).[52] The GGP was developed to provide more

[49] *Aventis Pharma Deutschland et al. v. Lupin Ltd. et al*., Civil Action No. 2 :05cv421, (U.S. District Court for the Eastern District of Virginia, 5 June 2006).
[50] Anne-Marie Slaughter, 'Disaggregated Sovereignty: Towards the Public Accountabiity of Global Government Networks' (2004) 39 Government and Opposition 159, 171, A.-M. Slaughter, *A New World Order* 218.
[51] For more on the ICH procedure see www.ich.org. See also A. Berman, ' Informal International Law-Making in Medical Products Regulation' in J. Pauwelyn, R. Wessel, J. Wouters (eds.) *Informal International Law-Making: Case Studies* (TOAEP, 2012) (forthcoming).
[52] 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

transparency, public participation and formality in the guidance development process.[53] According to the GGP, guidance documents "do not legally bind the public or the FDA", and an applicant "may choose to use an approach other than the one set forth in a guidance document". That said, guidance documents "represent the (FDA's) current thinking. Therefore, FDA employees may depart from guidance documents only with appropriate justification and supervisory concurrence".[54] In practice, despite their non-binding legal status, the ICH guidance documents *de facto* bind the pharmaceutical companies that develop drugs and apply for FDA approval. As these guidelines set out testing procedures, not following them would risk rejection by the FDA with costly outcomes for the companies.

Under the GGP, the draft ICH guideline is subject to a notice and comment procedure,[55] which is very similar to the general rule-making procedure set forth in the Administrative Procedure Act (APA).[56] The U.S. public takes advantage of these consultation opportunities, but the overwhelming majority of comments comes from industry.[57] To receive further input, the FDA may also hold public meetings or workshops, or present the draft to an advisory committee.[58]

Not only is the draft guidance document subject to notice and comment procedures, but domestic consultation can also be conducted *before* a first draft has been issued: Any new topic is published in the FDA's "guidance document agenda", which is open for public input.[59] Further, before preparing a draft guidance document, the FDA can seek or accept early public input,[60] or conduct public meetings or workshops.[61] And indeed, prior to every ICH meeting the FDA issues a notice in the Federal Register,[62] and holds a public meeting to update the public regarding ICH topics underway and to give an opportunity for public input.[63] The transcripts of these meetings are available online.[64] NGOs and industry representatives have been taking advantage of these

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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. Regarding the ICH: see Section 4.1.3. of the EMA Procedure.

[53] 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).

[54] 21 CFR §10.115 (d) (1)-(3).

[55] 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.

[56] Todd D. Rakoff, 'The Choice Between Formal and Informal Modes of Administrative Regulation' (2000) 52 Administrative Law Review 159, 168-169.

[57] According to the results displayed at www.regulations.gov.

[58] 21 CFR 10.115(g)(1)(iii)(A) and (B). For example, the FDA has conducted a public workshop to receive input from experts on the "ICH S2 Genetic Toxicology Issues" guidelines.

[59] 21 CFR 115(f)(5).

[60] 21 CFR 10.115(g) (1)(i).

[61] 21CFR 10.115(g)(1)(i).

[62] 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)

[63] 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.

[64] Transcripts of public meetings from recent years may be retrieved from www.regulations.gov.

meetings and attend them. For example, the International Council on Animal Protection, an NGO representing European, U.S. and Asian animal protection groups, has used this opportunity to express its desire to participate in the ICH when animal testing guidelines are being developed.[65]

After all comments gathered at the domestic level are transferred to the ICH's working group, a renewed consensus-building process takes place. The regulators exchange the domestic comments they have received in order to arrive at a single, harmonized guideline. This stage 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 is adopted by the Steering Committee, and adopted as a harmonized guideline. When this is then adopted as a final FDA guidance document, it is published in the Federal Register, and is 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 ICH's procedural rules lack a reason-giving requirement too. It is, hence, difficult for the public to discern the extent to which comments made at the domestic level have had an impact on the final ICH guideline.

Finally, it should be noted that the adoption of ICH guidelines as guidance documents follows a trend in the past two decades in U.S. federal agencies, including the FDA, to increasingly set purely domestic regulatory policy through guidance documents rather than binding regulations.[66] That is to say, the adoption of ICH guidelines as guidance rather than binding regulations follows an existing domestic trend rather than reflecting an exception.[67]

D. 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".[68] The problem is said to be that regulators active in transgovernmental networks are free from the political constraints and administrative legal limitations that typically apply to regulators. What role then does domestic administrative law have in keeping the network accountable to internal stakeholders? We next seek to provide an answer to this question.

1. Domestic Administrative Law as a Means of Ensuring Internal Accountability: Merits and Limitations

[65] S. Dhruvakumar, 'FDA CDER ICH Public Meeting' (20 April 2005)
[66] T. D. Rakoff, 'The Choice Between Formal and Informal Modes of Administrative Regulation' 165-166.
[67] This practice is also widespread in other countries, such as by the EMA.
[68] A.-M. Slaughter, 'Disaggregated Sovereignty: Towards the Public Accountabiity 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.

The findings of this paper demonstrate that the FDA's participation in harmonization networks is authorized under U.S. law, and recognized as part of the FDA's mission. Subsequently, in principle, stakeholders within the U.S. – the government, regulated industry actors and other diffuse 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 in and overseeing guidance development activities of the FDA that are purely domestic in character – a situation that Stewart refers to as "parity".[69]

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 on which the FDA will not be able to implement a guidance document, and hence will not agree to in a transnational negotiation, the network as a whole cannot consider this topic. This, accordingly, may keep the ICH's output in line with the interests of U.S. stakeholders. 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, 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 and the courts have not substantially dealt with the ICH. Moreover, while the commenting procedure is open to anyone interested, comments on FDA draft guidance documents based on ICH guidelines have largely come from the pharmaceutical industry, and very few have been made on behalf of consumers and patients.[70] 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 take advantage of them.

Second, while in principle domestic measures may have a limiting effect, there is a separate question as to how *meaningful* they are in keeping the regulatory authorities in check relative to the interests of the U.S. public. The literature, most notably Stewart, has doubted the power of domestic administrative law to provide meaningful accountability in connection with domestic implementation of global norms.[71] A central criticism concerning international harmonization has been that procedures for harmonization are far less open to public scrutiny and participation than domestic regulatory decisional processes.[72] Another criticism has been that the effective center

[69] R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 723.
[70] Revealed by a search of www.regulations.gov.
[71] R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 723.
[72] Ibid. 714.

of decision-making gravity lies outside of the agency, which in turn depreciates the value of domestic administrative law procedural requirements.[73] As we have seen, the facts of this case suggest otherwise. The procedures for developing harmonized guidelines are as open as those that apply to domestically developed guidance. Moreover, the *early* involvement of U.S. 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 working group sessions.

The decision to involve stakeholders during the actual development of the guideline in the ICH's working groups, together with regulators and industry, would have to be made at the ICH level. This clearly points to the conclusion that while domestic measures are important, and contribute to accountability, they are not enough. Accountability measures at the global level (for example, measures that would allow for such involvement in the working groups) are also 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.[74]

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

But even if the APA, rather than the GGP, procedures applied, the major problem remains that industry enjoys a preferential position in the TRN in comparison to the public (representing diffused social interests) participating in the domestic procedures: domestic procedures allow for *non-voting* participation of the public, whereas industry enjoys *voting-like* participation at the transnational level.[75] This results in unequal representation of interests in 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

[73] Ibid.719.
[74] See for a similar view, ibid. 754.
[75] 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.

standards or level of protection) and maximum regulatory alignment? Possible solutions for this imbalance would be the inclusion of representatives of diffused social interests, such as patient organizations, on an equal footing with industry within the TRN, or alternatively, removal of the preferential status industry enjoys by becoming a regulators-only network.[76]

Fourth, looking beyond the specific case at hand, the strength of the accountability mechanisms provided by domestic administrative law will depend to a large extent on the specific case at hand: 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 from which the regulator comes (different countries have different approaches as to the autonomy/accountability of their regulators), and the domestic procedural requirements for implementing transnational standards (for instance implementation as guidance documents rather than as legal regulations).

Higher levels of regulatory 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 stronger source of accountability than domestic administrative law in developing countries with less sophisticated domestic regulatory systems. [77] But even among developed high-income countries we see variations.[78]

To conclude, the ability of domestic administrative law to control regulators (and in turn the network) may be considerable, but it also has its limitations. What international lawyers should not overlook, however, is that this problem is not new, but rather a central problem inherent in the role of regulatory authorities within democratic countries.[79] Within any state, regulatory authorities lack a firm democratic basis as they are not elected, and so problems of accountability, when policy is made

[76] For further discussion of this topic, see A. Berman, ‘ The Public-Private Nature of Harmonization Networks’, (CTEI Working Paper 6/2011), available at http://graduateinstitute.ch/webdav/site/ctei/shared/CTEI/working_papers/CTEI-2011-06.pdf

[77] 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 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.

[78] 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.

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

at the greatest remove from political controls, are already rooted in the domestic administrative system.[80]

2. Insights for the Future

Given the conclusions outlined above, 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 could or should have in maintaining the accountability of regulators.

This then brings us to the question whether the particular characteristics of transnational harmonization (being more removed than domestic processes,[81] and subject to a requirement that the views of foreign regulators and industry associations be considered on an equal footing etc.) justify additional or specific domestic accountability measures beyond the existing ones, or what Stewart refers to as "parity plus"?[82] Phrased more generally: Is there a need to adapt our domestic administrative legal systems in order to maintain the accountability of our regulators in the face of globalization and their transnational collaborations?

This paper does not purport to answer this question. As always, there will be a need to balance matters of accountability and effectiveness in finding solutions. On the one hand, transnational collaboration adds to the equation of regulators' discretion additional elements that were previously not as significant, in particular the consideration of foreign and industry interests. Thus, in their transnational activities regulators should be required to reasonably balance between two conflicting interests: the advantages of harmonization and the protection of the (domestic) public interest. To this end, more or better domestic accountability measures to oversee them should be developed. On the other hand, increased domestic control will come at the cost of the transnational bargaining process, and will reduce the effectiveness of harmonization. Thus, we should be mindful of the advantages of effective collaboration and harmonization before adding more accountability measures.

Whatever stand one takes, and even if one were to take the stand that increased oversight is warranted, in practice, as we have seen, currently there does not seem to be much concern in the U.S. government. In other countries the approach seems to be slightly different. In Canada, for example, special requirements apply to regulators' transgovernmental activities. There, the *Guidelines on International Regulatory Obligations and Cooperation* issued by Canada's Treasury Board[83] support international regulatory cooperation, but at the same time expressly acknowledge the

[80]On the lack of traditional democratic accountability, see for example Susan Rose-Ackerman and P. Lindseth, 'Introduction ' in S. Rose-Ackerman and P. Lindseth (eds.), *Comparative Administrative Law* (Edward Elgar Cheltenham, UK 2010)7.
[81] R. B. Stewart, 'The Global Regulatory Challenge to U.S. Administrative Law' 728.
[82] Ibid.723,728.
[83] 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.

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",[84] 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."[85] It also requires Canadian regulators to "engage stakeholders when developing international obligations and international regulatory cooperation approaches and explain to interested and affected parties why cooperating with other governments or adopting international standards benefit Canadians."[86]

6. Domestic Administrative Law and External Stakeholders

We now turn to explore the role which domestic administrative law does, and could, play in ensuring the accountability of the harmonization network to, or in offsetting its disregard of, external stakeholders. One of the main criticisms of the ICH is that it is dominated by high-income countries and the innovative pharmaceutical industry, and its work has not taken into account the effects of ICH guidelines on developing countries. Have or could domestic administrative procedures offset the disregard of these stakeholders? We address this question below, but begin with a short overview of the ICH's main external stakeholders, with particular attention to developing countries.

A. Defining the External Stakeholders

1. Non-Member Countries that Adopt ICH guidelines

Two decades ago, when the ICH was first set up, the pharmaceutical market was almost exclusively dominated by the US, Europe and Japan. In the past decade or so, with globalization, the pharmaceuticals market is in the process of undergoing a major shift, and the manufacture of drugs has shifted to developing and emerging economies in Asia, Eastern Europe, and Latin America. These developments have generated a growing interest of non-ICH countries and industries in ICH guidelines. ICH guidelines have become *de facto* global standards that are being followed by many countries that are not members of the network. Drug developers and producers in non-member countries also tend to follow ICH guidelines, irrespective of whether the country in which they operate 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, 90% of which is controlled by ICH countries, 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

[84] Ibid. Section 2.1.
[85] Ibid.Section 2.1.
[86]Ibid. Section 3.1.2.

on ICH guidelines. They are wary of being accused of producing substandard pharmaceuticals, 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 driven only by government and industry, 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 trials follow the ICH guideline on clinical trials.[87] 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 roughly distinguish between three main groups:

(i) Developed countries, such as Switzerland, Canada or Australia. The pharmaceutical industry of these countries has traditionally been dependent on, and linked with, that of ICH members. These countries and their industries have, hence, traditionally adopted or relied on ICH guidelines.

(ii) So-called "pharmerging" countries, such as China, Brazil, Russia and India. With the shift of pharmaceutical production, industries in these countries have become significant producers of pharmaceutical materials – in particular active pharmaceutical ingredients (APIs), or have become active in conducting clinical trials. Thus, such countries have or are in the process of adopting/adapting ICH guidelines, in particular those of relevance to manufacture of active pharmaceutical ingredients (APIs), quality manufacture, and clinical trials.

(iii) Regional harmonization Initiatives (RHIs), defined as "initiatives harmonizing drug regulation across a defined group of non-ICH countries"[88]. The RHIs are the Asia-Pacific Economic Cooperation (APEC), the Association of Southeast Asian Nations Pharmaceutical Product Working Group (ASEAN PPWG),, the Gulf Cooperation Countries 'Gulf Central Committee for Drug Registration' (GCC-DR), the Pan American Network on Drug Regulatory Harmonization (PANDRH), the South African Development Community (SADC), and the East African Community (EAC). These countries –which include the above two groups as well as developing countries – have been adopting ICH guidelines too. These RHIs have been actively encouraging the adoption of ICH guidelines in their regions. For example, APEC has set

[87] Trudie Lang, Phaik Yeong Cheah, and Nicholas J. White, 'Clinical research: time for sensible global guidelines' (7 May 2011) 377 The Lancet 1553, 1554.
[88] "FAQS » at www.ich.org.

up the APEC Harmonization Centre (AHC) in 2010, which promotes the implementation of ICH guidelines in the Asia-Pacific region.[89]

2. The Effect of ICH Guidelines on the Political Economy of Developing Countries

The fact that non-member developing countries and their industries follow ICH standards raises two main concerns from a political economy perspective.

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 an ICH member). The generics industry is particularly important for developing countries, since most drug-production taking place in developing countries is of generics. Moreover, the main health concern of developing countries is the availability of essential drugs to its local population, and developing countries rely on generic drugs to ensure this; indeed in many developing countries, essential drugs required for the prevention and treatment of locally endemic conditions are not supplied by the major multinationals, but by local producers. 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.

As a result, 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. The impact of 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.[90] 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.

Second, the ICH guidelines on clinical trials were primarily written for commercially driven drug registration studies, and their requirements are unaffordable and unattainable in developing countries. Accordingly, the guidelines have been an

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[89] For further information about the ICH and external stakeholders, see A. Berman, ' Informal International Law-Making in Medical Products Regulation' in J. Pauwelyn, R. Wessel, J. Wouters (eds.) *Informal International Law-Making: Case Studies* (TOAEP, 2012) (forthcoming).

[90] 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 2, 21-24. See also 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, and WHO, 'Global Harmonization and the ICH' Essential Drugs Monitor (2001) http://apps.who.int/medicinedocs/en/d/Jh2977e/4.html, accessed 9.

impediment to clinical research in developing countries, with potential adverse effects on the development of drugs for local needs.[91]

The fact that adoption of "western" standards in developing countries may have political economy effects goes beyond the ICH's case and is relevant to other harmonization networks. This problem is related to the fact that western standards incorporate a certain risk/benefit ratio that may not appropriately reflect the needs of developing countries. For example, the Basel Committee's capital adequacy requirements have also been said to create major challenges for developing countries.[92]

The question, then, is what role domestic administrative law could or should have in solving this problem. But first we provide a short overview of the accountability measures available at the transnational level.

B. Accountability Measures at the Transnational Level

At the ICH level, accountability-promoting measures towards external stakeholders exist and are continuously being introduced.

Originally, the ICH was set up as a club, limited to the US, Europe and Japan. Following the globalization of the pharmaceutical market, the ICH governance structure has undergone several adaptations. The ICH has set up two "outreach" bodies that allow for communication with non-member countries: The 'Global Cooperation Group' brings together the RHIs mentioned above and drug regulatory authorities (DRAs) from countries with a tradition of using ICH guidelines or an intention to do so, or from countries that are a source of APIs, medical products or clinical data for the ICH regions (currently, Australia, Brazil, China, Chinese Taipei, India, Russia, Singapore and South Korea). The GCG's main purpose is to serve as a conduit for disseminating ICH guidelines to the non-members. The 'Regulators Forum' consists of regulatory authorities only from the ICH member regions, the observers, the RHIs, as well as the other DRAs just mentioned. The ICH has also welcomed RHIs and DRAs as non-voting participants in expert working groups.

Furthermore, the IGPA, an association of generic medicines manufacturers from the EU, Canada, U.S., Japan and India, has also been accepted as an "interested party", and participates in expert working groups of relevance to its work.[93] Developed countries such as EFTA members, Switzerland and Health Canada have been observers since the ICH was first set up. The WHO is an observer too, and is tasked with bringing the interests of those countries that are not ICH members to the table.

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[91] T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1554.
[92] 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
[93] e.g. Expert working group on 'Development and Manufacture of Drug Substances : Q11' (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/Concep_Paper/Q11_Concept_Paper.pdf accessed 11 October 2011.

Without going into the details, transnational accountability measures play an important role in keeping the ICH accountable towards external stakeholders. [94] But the purpose of this paper is to explore the role of domestic measures, and therefore we ask: 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.[95] Is that indeed the case?

C. Domestic Administrative Law in Member Countries

Notice and comment procedures in U.S. rule making or guidance development are open to "all affected parties outside of FDA",**[96]** including foreigners.**[97]** 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 public meetings before ICH meetings are a conduit for input by non-ICH organizations into the ICH process.**[98]** The use of domestic procedures may, therefore, be a tool for external stakeholders to voice concerns.

We see this approach of openness towards foreign stakeholders within the domestic administrative systems of 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.[99] In fact, this approach is part of the regulatory reform many OECD and APEC countries have undergone in the past decade. The "APEC–OECD Integrated Checklist for Regulatory Reform", which reflects regulatory reform principles developed since the 1990s 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,*[100] and that foreign parties

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[94] For a more encompassing oversight of these measures, see A. Berman, ' Informal International Law-Making in Medical Products Regulation' in J. Pauwelyn, R. Wessel, J. Wouters (eds.) *Informal International Law-Making: Case Studies* (TOAEP, 2012) (forthcoming).

[95] See R. B. Stewart, 'Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance (Draft Paper)' 38.

[96] 21 CFR 10.115 (c)(3).

[97] 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.

[98] 'FDA ICH Public Meeting' (20 October 2005) http://www.regulations.gov/#!documentDetail;D=FDA-2005-N-0395-0002.

[99] 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> accessed 11 Oct. 2011.

[100] Principle A6 of the OECD/APEC, 'OECD-APEC Integrated Checklist for Regulatory Reform' http://www.oecd.org/dataoecd/41/9/34989455.pdf accessed 11 Oct. 2011.

be allowed to comment[101] and access appeal systems.[102] 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."[103]

Moreover, agreements concerning foreign participation in consideration of regulatory measures have been concluded between countries such as the U.S. and the EU,[104] and the U.S., Mexico and Canada.[105] And indeed, we find, for example, rules on consultation with foreign regulatory authorities in the EMA's Guideline Development Procedures,[106] and in Canada.[107]

To conclude, domestic law in the U.S. makes certain accountability measures 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. In cases of fundamental clashes between the FDA and foreign interests, such domestic procedures would most likely be meaningless.

In any case, 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 U.S. companies' products and clinical research, submitted to the FDA comments regarding ICH guidelines on clinical trials.[108] Another example is the Association of the British Pharmaceutical Industry, which provided comments to the FDA concerning an ICH genotoxicity guideline.[109] 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 (but also to the EMA and the JPMDA). In the absence of reason-giving for acceptance or rejection of comments, it is difficult to establish whether these comments have had any effect on the final guidelines.

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[101] Ibid. principle D5.
[102] Ibid. principle A11.
[103] 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.
[104] s. 4, 17 Transatlantic Economic Partnership, 'Guidelines on Regulatory Cooperation and Transparency' (2002) http://ec.europa.eu/enterprise/policies/international/files/guidelines3_en.pdf.
[105] 'Canada/United States/Mexico Security and Prosperity Regulatory Cooperation Framework'
[106] s. 4.7 European Medicines Agency, Procedure for European Union Guidelines and Related Documents within the Pharmaceutical Legislative Framework.
[107] s. 4 Treasury Board of Canada, 'Guidelines for Effective Regulatory Consultations'
[108] Latin American Forum for Ethics Committees for Health Research (FLACEIS), '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.
[109] 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.

D. Domestic Administrative Law in Non-Member Countries

Domestic administrative law within non-member states could have a role in compensating for the problem of disregard at the global level. This is the case in the ICH, but also more generally in connection with other harmonization networks.

Domestic administrative procedures may serve 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 the consent of non-members is not required for consensus, the domestic administrative law of non-member countries does not 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 the considerations of non-member countries into account (a weak accountability measure nevertheless?).

In any case, many non-member countries are indeed relying on domestic administrative procedures to serve these two functions. In many developed non-member countries, such as 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 of ICH guidelines.[110] China's State Food and Drug Administration, an emerging administration, has set up an "ICH research guideline group", which is intended to study ICH guidelines, compare them with Chinese guidelines, and adapt the latter while maintaining local needs.[111] 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 phenomenon 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

[110] 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-GCG_Reports/Nov_2008_Brussels/DRA_Australia_Presentation_in_Brussels.pdf> accessed 11 October 2011.

[111] 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> accessed 11 October 2011.

preferences. A one-size-fits-all approach rarely works and global standards will often need to undergo domestic adaptation, if not *de jure*, than certainly *de facto*.[112]

Arguably, domestic procedures could have a role to play in offsetting the problem of disregard of 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 that preferred by the high-income countries driving ICH guidelines,[113] local adaptation seems promising. In a sense developing countries would be free-riding on goods (the scientific information embedded in the guidelines) produced by well-resourced countries, and would only need to invest in adapting them to their needs. Since ICH guidelines are 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 would not be undermined.[114]

That said, in practice, there are several limitations to the potential for domestic law as a tool to offset the problem of disregard. First, as the market is dominated by ICH countries, if non-member countries wish to remain globally competitive (and to be able to sell into the big ICH markets), their guidelines cannot 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

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[112] 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 situations. Yane Svetiev, 'The Limits of Informal International Law: Enforcement, Norm-generation and Learning in the ICN' in J. Pauwelyn, R. Wessel, and J. Wouters (eds.), *Informal International Lawmaking* (Oxford University Press, Oxford 2012 (forthcoming))

[113] Vesna Koblar, 'Impact of ICH on Non-ICH countries ' (Tenth International Conference of Drug Regualtory 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 P. accessed 11 October 2011.

[114] 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.

adaptation unfeasible.[115] The third concern is that in some cases, local adaptation could lead to double standards between "western" and "third world" standards,[116] 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 adapted guidelines might be regarded as inferior.[117]

In reality it will often be the case that the local drug regulatory authority formally adopts the international guideline but, as the standards are unattainable for local producers, does not enforce the international guideline in practice. This is the case, for example, in Tanzania, where local authorities formally adopt international standards, but for industrial policy purposes, support local producers by not enforcing them.[118] 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 us to a conclusion that, in order to improve the network's accountability to its external stakeholders, the best way would be to involve their interests at the transnational level. As mentioned above, this process is partly underway in the ICH, such as by setting up the Global Cooperation Group, the Regulators Forum and including non-members in the expert working groups. These organs, however, are mostly focused on disseminating ICH globally, rather than addressing the interests of non-members.

But even if more appropriate transnational accountability measures were to be set up, it should be kept in mind that a *prerequisite* to the transnational involvement of developing countries is the existence in such countries of a functioning drug regulatory authority.[119] But regulatory capacity is low in developing countries. In Africa, for example, the overwhelming majority of African drug regulatory authorities lack capacity and resources.[120] Thus, efforts to improve accountability to developing countries should be combined with aiding these countries in developing domestic regulatory capacities. For accountability to be meaningful at the transnational level, it must be bound up with the notion of development. This is the foundation that will eventually lead to greater accountability.

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[115] T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1555.
[116] V. Koblar, 'Impact of ICH on Non-ICH countries '.
[117] T. Lang, P. Y. Cheah, and N. J. White, 'Clinical research: time for sensible global guidelines' 1554.
[118] 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)
[119] 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.
[120] 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.

An alternative solution would be 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 already demanded, or it would independently develop more sensible guidelines on the basis of ICH guidelines. The RHIs mentioned above – APEC, ASEAN, GCG etc. – to a large extent indeed take up this role and represent developing countries with low regulatory capacities before the ICH. Such collective, rather than individual, representation is also more effective.

7. Conclusion

This paper has explored the role played by domestic law 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 "extraterritorial" rules are set by powerful member states, whose participation in the network is important in order for the network to achieve its purpose, 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 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 to internal stakeholders. In thinking about the future, and in maintaining the accountability of regulators in face of globalization, countries should consider strengthening or improving the domestic accountability measures that apply to the transnational activities of their regulators.

However, domestic measures can only work up to a point. In order to achieve better accountability to internal stakeholders, domestic measures must be complemented by accountability measures at the transnational level. Only a combination of both will allow for meaningful accountability to 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.

Third, as regards external stakeholders, domestic administrative law in the U.S. (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 could theoretically allow for adaptation of transnational standards to local needs. In this case administrative law does not serve so much as an accountability measure, but rather as a tool to tailor transnational standards to the local context. In practice, this approach can really only make a difference in relation to standards for purely local research and production, and even in this regard faces several problems. Consequently, while domestic administrative law has some potential as a means of addressing the problem of disregard of external stakeholders and their needs, its

contribution can only be limited. The interests of non-member countries need to be taken into account at the transnational level. This conclusion is shared by others who have argued that domestic accountability procedures do not solve the problem of disregard. [121]

The difficulty with this conclusion is that accountability measures at the transnational level may not be meaningful if a country does not have domestic regulatory institutions in place that can participate in transnational processes. Domestic regulatory capacity is a *precondition* for accountability at the transnational level. The interests of countries which lack a functioning regulatory system capable of even minimal participation in transnational forums may need to be represented by "surrogates" such as intergovernmental organizations, NGOs or RHIs. RHIs indeed currently play an important role in the ICH.

To conclude, domestic law is an important means of improving the accountability of TRNs to internal stakeholders, and has some role, albeit limited, in offsetting the problem of disregard of external stakeholders. Accountability measures at the transnational level remain important too. They may improve accountability to internal stakeholders, and are critical when it comes to external stakeholders.

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