

GLOBAL PHARMACEUTICAL STANDARDS: A NEW REGULATORY PARADIGM?

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ABSTRACT

One of the constant features of legal scholarship in the past few years has been an increasing attention paid to what is usually described as the transformation of global regulatory experience. Evidence of such transformation which is commonly pointed to includes the fragmentation of rule-making processes, the lack of legitimacy of decision-making, increasing de-differentiation between legally binding rules and voluntary rules of conduct and so on. This paper aims to test the transformation thesis in light of a particular example of global pharmaceutical standards. More specifically, the research task which is being addressed in this paper is to determine the extent to which global pharmaceutical standards depart from the traditional regulatory paradigm at the international level. My research hypothesis is as follows: while global pharmaceutical standards testify to the transformation of traditional regulative frameworks, it seems, on a closer examination, that the thesis of radical departure from traditional regulatory paradigm which has been at work in the global arena needs to be qualified. For instance, although technically voluntary, pharmaceutical standards enjoy a significant degree of practical efficiency. At first sight, this can be seen as a remarkable novelty as a matter of regulatory philosophy. However, it seems that reasons which account for such a phenomenon have been at work in what is conceived of as traditional regulatory experience. Similar remarks can be offered as regards the sort of legitimacy that pharmaceutical standards enjoy because of the authority of science in modern societies.

By “re-familiarizing” pharmaceutical standards in this way, I do not intend to deny that they pose various new practical and conceptual challenges. My aim is simply to show that these standards also exhibit some features which can be traced back to more traditional legal experience. Although the focus of this paper is primarily analytical, such a theoretical prospect is not devoid of practical interest: as is well known, proper identification of a problem is central to its successful resolution.

On a more practical note, the paper is still a work in progress and as such remains incomplete in many respects: arguments are not always fully developed; some issues need to be taken up in more details and so on. I hope however that the paper conveys enough to generate discussion, suggestions and criticisms.

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INTRODUCTION

The transformation of the global regulatory landscape has been a common theme in the literature on international law and international relations over the past few years.¹ Numerous features of that transformation have been highlighted, ranging from the polycentric nature of regulative frameworks to their hybrid or private-sector origins and lack of accountability or legitimating mechanisms.² For some, the phenomenon in question is to be characterized as a consequence of globalization.³ Although there is some truth in such an outlook, one should not overlook the fact that some elements of the transformation of international legal experience were arguably present even before the era of globalization began. To take but one example, techniques of international legal regulation have undergone major transformations in the last hundred years to the extent that it seems impossible to contend nowadays that Article 38 of the ICJ Statute, which has traditionally been taken as containing a comprehensive list of the sources of international law, provides an accurate picture of the legal regulation at the international level. As emphasized in a recent treatise “law-making is no longer the exclusive preserve of states”.⁴ Far from being limited to the formal dimension of international law, transformation of international law has also concerned the substance of the latter. It can no longer be contended that international law is a value-neutral legal system designed to ensure the coexistence of independent political entities as the Permanent Court of International Justice once held.⁵ Evolution of functional needs at the international level has transformed international law from a coexistence-centered to a cooperation-promoting system.⁶

¹ See, e.g., Christian Brüttsch & Dirk Lehmkuhl (eds.), *LAW AND LEGALIZATION IN TRANSNATIONAL RELATIONS* (Oxford / New York: Routledge, 2007); Jean Clam & Gilles Martin (eds.), *LES TRANSFORMATIONS DE LA RÉGULATION JURIDIQUE* (Paris, LGDJ, 1998).

² See, e.g., José E. Alvarez, *INTERNATIONAL ORGANIZATIONS AS LAW-MAKERS* (Oxford: Oxford University Press, 2006); Thomas Biersteker & Rodney B. Hall (eds.), *THE EMERGENCE OF PRIVATE AUTHORITY IN GLOBAL GOVERNANCE* (Cambridge University Press, 2002); Claire A. Cutler, Virginia Haufler & Tony Porter (eds.), *PRIVATE AUTHORITY AND INTERNATIONAL AFFAIRS* (New York: SUNY Press, 1999); Daniel W. Drezner, *ALL POLITICS IS GLOBAL: EXPLAINING INTERNATIONAL REGULATORY REGIMES* (Princeton University Press, 2008); Benedict Kingsbury, Nico Krisch & Richard B. Stewart, *The Emergence of Global Administrative Law*, 68 *LAW & CONTEMPORARY PROBLEMS* (2005) 15-61; Käl Raustiala, *The Architecture of International Cooperation: Transgovernmental Networks and the Future of International Law*, 43 *VIRGINIA JOURNAL OF INTERNATIONAL LAW* (2002) 1-92; Anne-Marie Slaughter, *A NEW WORLD ORDER*, Princeton University Press, 2004; Pierre-Hugues Verdier, *Transnational Regulatory Networks and Their Limits*, 34 *YALE JOURNAL OF INTERNATIONAL LAW* (2009) 113-172; David Zaring, *International Law by Other Means: The Twilight Existence of International Financial Regulatory Organizations*, 33 *TEXAS INTERNATIONAL LAW JOURNAL* (1998) 281-330.

³ See, e.g., Karim Benyekhlef, *UNE POSSIBLE HISTOIRE DE LA NORME: LES NORMATIVITÉS ÉMERGENTES DE LA MONDIALISATION* (Montréal: Editions Thémis, 2008).

⁴ Alan Boyle & Christine Chinkin, *THE MAKING OF INTERNATIONAL LAW* (Oxford: Oxford University Press, 2007) at vii.

⁵ *Lotus (Turkey v. France)*, 1927 P.C.I.J. (ser. A) No. 10, 4, 18 (Sept. 7).

⁶ This, in turn, has impacted techniques of international legal regulation. As George Abi-Saab observed, building on Wolfgang Friedmann’s work (Wolfgang Friedmann, *THE CHANGING STRUCTURE OF INTERNATIONAL LAW* (Columbia University Press, 1964), the emergence of ‘soft law’ at the international level was, for instance, intimately connected to the structural changes of international law: a law whose focus is no longer on the mere coexistence of its various subjects, but on the active cooperation among them and designed to achieve some common goals cannot proceed exclusively by means of prescriptions and needs regulatory tools of a recommendatory nature (George Abi-Saab, *Eloge du droit assourdi. Quelques réflexions sur le rôle de la soft law en droit international contemporain*, in *NOUVEAUX ITINÉRAIRES EN DROIT: HOMMAGES A FRANÇOIS RIGAUX*, Bruxelles, Bruylant, 1993, at 59).

The inescapable conclusion seems to be, that – to paraphrase Sir Gerald Fitzmaurice⁷ – change cannot be conceived as a novelty in international law. Law – including international law – is a social phenomenon designed to regulate a specific set of social relations. There is, therefore, nothing remarkable in the fact that changes in social relations reflect in law.⁸

It is, however, tempting to think that the transformation of the global regulatory experience we have been witnessing in the last decades is of a special kind to the extent that it cannot be compared to the ordinary, incremental change of legal experience in response to societal changes. For one thing, such transformation has not been limited merely to the sphere of international law, as domestic laws have been experiencing the same sort of metamorphosis as to its paradigmatic features. The scope of the transformation also seems unprecedented because what are ordinarily seen as central features of legal phenomenon have been changing to a significant extent. This explains why the alternative explanation, which sees the transformation of law as a consequence of a larger process of change whereby our “form of life”⁹ has moved from modernism into postmodernism, enjoys a significantly higher level of support.

This paper aims to test this explanation in light of a particular example of global pharmaceutical standards which are designed to ensure the quality and safety of pharmaceuticals, the research question being to determine the extent to which they depart from the traditional regulatory paradigm at the international level.

Before engaging in a substantive discussion of the impact of global pharmaceutical standards on the legal phenomenon at the international level, it is important to provide a working definition of standards. Although global standards have been characterized as “pervasive mechanisms of international governance”¹⁰, the term “standard” is not used in the literature in a coherent fashion.¹¹ There seems to be an agreement at a fairly general level that “a standard is a guide for behavior and for judging behavior”.¹² However, the term is sometimes used to refer to any normative guide designed to govern a conduct, including traditional “hard law” rules.¹³ In this paper I use the term “standard” in a more specific sense referring to a particular type of tool of regulation. There are several definitions provided in international instruments which can serve as a starting point. An example is Annex 1.2 of the TBT Agreement which

⁷ Sir Gerald Fitzmaurice, *The Future of International Law and of the International Legal System in the Circumstances of Today*, in ANNUAIRE DE L’INSTITUT DE DROIT INTERNATIONAL, Livre du Centenaire, Bâle, Karger, 1973, at 207.

⁸ Jacques Chevallier, *Vers un droit post-moderne? Les transformations de la régulation juridique*, 3 REVUE DU DROIT PUBLIC, (1998) at 660.

⁹ I use the term in the sense introduced by Ludwig Wittgenstein (PHILOSOPHICAL INVESTIGATIONS, Oxford, Basil Blackwell, 1967, paras, 19, 23, 241) which roughly refers to significant patterns in our lives. See J.F.M. Hunter, “Forms of Life” in *Wittgenstein’s Philosophical Investigations*, in E.D. Klemke (ed), ESSAYS ON WITTGENSTEIN (Urbana: Univ. of Illinois Press, 1971) at 273.

¹⁰ Kenneth W. Abbott & Duncan Snidal, *International ‘Standards’ and International Governance*, 8 JOURNAL OF EUROPEAN PUBLIC POLICY (2001), 345, at 347.

¹¹ A point of vocabulary needs to be mentioned at the outset. Standards as defined in this paper are sometimes referred to as “guidelines”, “norms” or “recommendations” (see, for instance, article 3.2 of the WTO SPS Agreement and the SPS Committee’s discussion relating to that provision, WTO, “Clarification of References to Codex Texts”, G/SPS/W/86/Rev.1). To the extent that these terms designate the phenomenon of standardization as described in this paper, I will take them to be interchangeable.

¹² Abbott & Snidal, *supra* note 10.

¹³ Herbert V. Morais, *The Quest for International Standards: Global Governance v. Sovereignty*, 50 U. KAN. L. REV. (2001-2002), 780, at 781 (discussing the evolution of human rights standards from a “soft law” instrument - the Universal Declaration of Human Rights - to the International Covenants on Human Rights).

defines a “standard” as a “document approved by a recognized body, that provides, for common and repeated use, rules, guidelines or characteristics for products or related processes and production methods, with which compliance is not mandatory. It may also include or deal exclusively with terminology, symbols, packaging, marking or labeling requirements as they apply to a product, process or production method”.¹⁴

Another widely used definition is offered in the ISO/IEC Guide 2 which defines “international standard” as a “standard that is adopted by an international standardizing/standards organization and made available to the public”.¹⁵ More helpfully, the Guide defines a “standard” as a: “document, established by consensus and approved by a recognized body, that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievement of the optimum degree of order in a given context”.¹⁶

The above definitions focus on the function, or the procedure of elaboration of standards. More important for our purposes are some distinctive characteristics of standards which highlight their peculiarity as a tool of global governance. First of all, standards are voluntary: in contrast to what happens with legal rules, compliance with standards is not mandatory.¹⁷ As explained by Arts and Kerwer, “[s]tandardizing ... [is] a form of regulation based on the attempt to influence others by voluntary rules”.¹⁸ This is not to suggest that standards are not, in fact, followed, nor does it mean that standards cannot be made mandatory. What this means is that a standard, in and of itself, does not create a legally binding commitment.

Another feature of standards is that they constitute more “an untidy regulatory mass without center or hierarchy”¹⁹ than a coherently structured system of regulations. Global standards are produced by multiple entities ranging from intergovernmental institutions to transnational or purely private bodies without their being any overarching organizing principle.

Mention must also be made of another characteristic of standards. Standards are guidelines based upon a technical or scientific expertise in a particular area. This is worth emphasizing for many reasons. To start with, this feature of standards arguably set them apart from legal rules. While a legal rule is ordinarily not a matter of necessity to the extent that it could well have been otherwise, a standard is built on the basis of technical or scientific knowledge and accordingly, does not present itself as a matter of

¹⁴ World Trade Organization, Agreement on Technical Barriers to Trade (TBT), Annex 1.2 (Definitions).

¹⁵ As a WTO Panel recently explained in the *Tuna II* case: *United States — Measures Concerning the Importation, Marketing and Sale of Tuna and Tuna Products*, WT/DS381/R (Complainant: Mexico), 15 September 2011, para. 7.664. In that case one of the issues was whether some provisions of the tuna tracking and verification and dolphin-safe certification resolutions adopted within the Agreement on the International Dolphin Conservation Program can be considered “international standards”, this definition brings to light characteristics of an international standard: it is a standard set forth by an international standard-setting body and made available to the public.

¹⁶ ISO/IEC Guide 2:2004 - Standardization and related activities -- General vocabulary.

¹⁷ Kristina Hallström, *ORGANIZING INTERNATIONAL STANDARDIZATION: ISO AND THE IASC IN QUEST OF AUTHORITY* (Northampton, Edward Elgar, 2004) at 29.

¹⁸ Bas Arts & Dieter Kerwer, *Beyond Legalization? How Global Standards Work*, in Christian Brüttsch & Dirk Lehmkuhl (eds.), *LAW AND LEGALIZATION IN TRANSNATIONAL RELATIONS* (Oxford / New York, Routledge, 2007) 144, at 145.

¹⁹ Benedict Kingsbury & Richard B. Stewart, *Legitimacy and Accountability in Global Regulatory Governance: The Emerging Global Administrative Law and the Design and Operation of Administrative Tribunals of International Organizations*, in *INTERNATIONAL ADMINISTRATIVE TRIBUNALS IN A CHANGING WORLD* (Spyridon Flogaitis, ed., Esperia, 2008) at 5.

choice but as a matter of unavoidable necessity if one is to achieve the specific goal that the standard seeks to attain. The fact that standards are supported by a specialized technical or scientific expertise also provides them with a type of legitimacy which is different from the one that legal rules are traditionally said to enjoy.

All this may seem familiar to any reader who has been exposed to discussions among legal theorists about the rise of a postmodernist paradigm of law which has supposedly replaced, or at least, seriously undermined, the traditional modernist picture of law. A brief summary of the terms of such debates may be in order.

It is relatively unproblematic to define modernism, since it is an intellectual framework which has been with us for a long time.²⁰ Modernism relies on Enlightenment philosophy and its unbridled trust in the power of reason.²¹ The implications of modernism for law are also easily understandable, since the whole conceptual world of law, at least, as the latter is ordinarily understood in the Western world, is organized around a certain number of modernist presuppositions. The assumption that the law constitutes an internally coherent system both formally and substantially, the certainty with which the distinction between law and non-law is operated, trust in the possibility of coherent legal structures and the power of reason to settle any substantial disagreements, and confidence in the power of organizing rational principles are among the most important of these implications.

Defining postmodernism is much more complicated, not least because there is no generally agreed definition in the vast literature on postmodernism and its implications for various fields of culture²². However, there is no need to engage with highly abstract definitional controversies given that there is already a consensus on the features of postmodernism which are deemed relevant for law.²³ At the inevitable risk of oversimplification, those features can be described as follows.

The most frequently aired characteristic of postmodernism is that it constitutes a framework in which “ephemerality and fragmentation take precedence over eternal truths and unified politics”.²⁴ As far as law is concerned, two important consequences can be seen to derive from this characteristic. First, it is impossible to ground postmodern law on stable substantive goals given that contemporary societies are highly complex and heterogeneous and that they simultaneously pursue mutually incompatible objectives. Second, whereas modernist law rests on monocentrism, postmodern law is characterized by its fragmentary nature. In modernism all law comes from “legislative reason”²⁵ and undergoes what has been termed a process of “positivization”²⁶ since public authority structures have a monopoly on legal

²⁰ See Anthony Giddens, *THE CONSEQUENCES OF MODERNITY* (Stanford: Stanford University Press, 1990).

²¹ Isaiah Berlin, *THE ROOTS OF ROMANTICISM* (Princeton: Princeton University Press, 2001) at 19-21.

²² See, e.g., Zygmunt Bauman, *INTIMATIONS OF POSTMODERNITY* (London: Routledge, 1992); David Harvey, *THE CONDITION OF POSTMODERNITY* (Oxford: Blackwell, 1989); Andreas Huyssen, *Mapping the Postmodern*, 33 *NEW GERMAN CRITIQUE* (1984) 5-52; Jean-François Lyotard, *THE POSTMODERN CONDITION: A REPORT ON KNOWLEDGE* (Manchester: Manchester University Press, 1984).

²³ See, e.g., Chevallier, *supra* note 8; Alan Hunt, *The Big Fear: Law Confronts Postmodernism*, 35 *MCGILL LAW JOURNAL* (1990) 507-540; Denis Patterson (ed.), *POSTMODERNISM AND LAW* (Darmouth: Aldershot, 1994); Helen Stacy, *POSTMODERNISM AND LAW* (Aldershot: Ashgate, 2001); Boaventura de Sousa Santos, *Law: A Map of Misreading. Toward a Postmodern Conception of Law*, 14 *JOURNAL OF LAW AND SOCIETY* (1987) 279-302.

²⁴ Harvey, *supra* note 22, at 327-328.

²⁵ Bauman, *supra* note 22, at 115-116.

²⁶ Niklas Luhmann, *A SOCIOLOGICAL THEORY OF LAW* (London: Routledge, 1985) at 147-158.

production. In contrast, postmodern law is pluralistic in the sense that its production is not confined to public structures and involves substantial participation of private actors as well as self-regulating structures. This explains why postmodern law cannot be described as a unitary, internally coherent system.

Do global pharmaceutical standards testify to such transformation of global regulatory paradigms? The present paper seeks to answer this question and analyze global pharmaceutical standards in order to determine to what extent they depart from the traditional regulatory paradigm at the international level. My research hypothesis is as follows. While global pharmaceutical standards no doubt provide an illustration of the transformation of traditional regulative frameworks, it would be misleading to think that the logic of their functioning exhibits *consistently* a radical departure from traditional modes of regulation in the global arena. In showing this, the research project aims to demonstrate that, contrary to conventional wisdom, the global regulative frameworks do not fit neatly into any single conceptual model. Identifying differing and sometimes conflicting trends simultaneously at work in the international regime of pharmaceutical standards, the present project purports to bring to light the complexity of current global regulatory regimes and therefore contribute to a better understanding of them.

The paper will proceed as follows. Part I will provide a brief explanation of why global pharmaceutical standards are functionally needed in view of the regulatory divergences between national systems. Part II will present the principal regimes of pharmaceutical standards in order to illustrate the multiplicity and complexity of the regimes involved. In Part III I set out to examine to what extent global pharmaceutical standards testify to the transformation of regulatory paradigms at the international level.

I. Overview of Regulatory Regimes for Pharmaceuticals

A proper understanding of the implications of global pharmaceutical standards requires providing some context for drug regulations. This part of the paper aims at providing such a context without going into the details which are not central to the main theme of the paper. Two aspects of drug regulations are worthy of notice in this regard. On the one hand, drug regulations are understandably part of national regulatory activities (A). On the other hand, the global reach of diseases and medicines makes it unrealistic to confine risk regulation activities to the limits of national borders (B).

A. Domestic Regulations and Therapeutic Cultures

Pharmaceutical products exhibit a much-noticed paradox. They are obviously an object of commercial interests: one needs go no further than the fact that there is such a thing as pharmaceutical industries the most important of which are held by multinational companies. At the same time, to the extent that no public health policy can possibly be conceived of without pharmaceutical products, those products are

also public goods designed to achieve publicly pursued and valued goals.²⁷ This paradox explains why pharmaceutical products are among the most heavily regulated products in every country. From the moment at which a pharmaceutical substance is discovered up to the moment at which it is commercialized a period of 8 to 12 years may elapse in the course of which such substance is tested on various respects.²⁸ Marketing authorization can only be accorded with respect to pharmaceutical products which meet the required level of safety and efficiency, as defined on the basis of technical guidelines or standards, to the satisfaction of the respective drug regulation authorities. Coupled with necessary enforcement measures to ensure that only registered medicines are traded, marketing authorization is a crucial dimension of any drug regulation policy.²⁹

The reason behind such an exercise of public authority over pharmaceutical products resides in the need to protect population from both diseases and dangerous and inefficient drugs.³⁰ Although this *rationale* is common to all countries, drug regulations vary from one country to another. Many reasons account for such disparity. Obviously, the level of economic development achieved by a given country is an important parameter. Building an effective regulation of medicines in developing countries is a major challenge, because resources and technical expertise are lacking, and many other pressing health needs compete for priority.³¹ Moreover, weak regulatory capacity is associated with a higher prevalence of substandard medicines. Even where regulations exist on paper, the inability of regulators to enforce the regulations properly may result in the trade in, and consumption of, substandard or falsified medicines.³²

Another reason is related to the divergence between national administrative traditions. National regimes of risk regulation reflect the historical background and technicalities of each administrative system. Each country possesses a discernable “therapeutic culture” of its own based upon “the historical evolution of a distinctive set of institutionalized relationships among the state, industry, physicians, and disease-based organizations”.³³ Such divergence between national drug regulations entails the necessity of an international cooperation with regard to pharmaceuticals.

²⁷ Kristina M. Lybecker, *Setting Priorities: Pharmaceuticals as Private Organizations and the Duty to Maximize Profits*, in Jillian C. Cohen (ed.), *THE POWER OF PILLS: SOCIAL, ETHICAL AND LEGAL ISSUES IN DRUG DEVELOPMENT, MARKETING AND PRICING* (London: Pluto Press, 2006) at 25 (“The pharmaceutical industry has an important social contract with the public to discover and develop medicines that have value in extending and enhancing life. Simultaneously, the industry must maintain its profitability, both to ensure the future stream of innovation and to provide investors with a return”); See also Thomas A. Faunce, *Toward a Treaty on Safety and Cost-effectiveness of Pharmaceuticals and Medical Devices: Enhancing an Endangered Global Public Good*, 2 *GLOBALIZATION AND HEALTH* (2006) at 3.

²⁸ John A. Vernon, Joseph H. Golec, Randall Luter & Clark Nardinelli (2009), *An Exploratory Study of FDA New Drug Review Times, Prescription Drug User Fee Acts, and R&D Spending*, 49 *QUARTERLY REVIEW OF ECONOMICS AND FINANCE* (2009) 1260-74.

²⁹ Goa Xia-Yun, *An Introduction to Administrative Protection for Pharmaceuticals*, 9 *DUKE JOURNAL OF COMPARATIVE & INTERNATIONAL LAW* (1998) 259, at 262.

³⁰ Alessandro Spina, *The Regulation of Pharmaceuticals Beyond the State: EU and Global Administrative Systems*, in E. Chiti & B.G. Mattarella (eds.), *GLOBAL ADMINISTRATIVE LAW AND EU ADMINISTRATIVE LAW* (Berlin: Springer-Verlag, 2011) at 249.

³¹ The WHO estimates that 30 per cent of countries have inadequate medicines regulation or none at all (WHO, *Effective Medicines Regulation: Ensuring Safety, Efficacy and Quality*, 7 *WHO POLICY PERSPECTIVES ON MEDICINES*, 2003). At a 2009 meeting, African regulators noted that an estimated 63 per cent of the 46 countries in sub-Saharan Africa had minimal medicines regulatory capacity and that 30 per cent had no drug regulatory authority. (WHO/AFRO, *First African Medicines Regulatory Authorities Conference - Final Report*, WHO Regional Office Africa, 2009).

³² Oxfam, *Eye on the Ball: Medicine Regulation Can Best Deliver Quality Medicines*, Oxfam Briefing Paper, 2011.

³³ Arthur A. Daemmrich, *PHARMACOPOLITICS: DRUG REGULATION IN THE UNITED STATES AND GERMANY* (Chapel Hill: University of North Carolina Press, 2004) at 4.

B. International Risk Regulation

Risk regulation at the international level is a response to a series of needs. First of all, as mentioned above, pharmaceutical products are goods which can be commercialized and as such, can be an object of import or export activities.³⁴ Since pharmaceutical products are also public goods and consequently bring into play public health considerations, a solution is to be found as to how the requirements of national drug regulations can be applied to transnational pharmaceutical activities.

Another factor which has contributed to the internationalization of drug regulations is globalization.³⁵ The phenomenon of globalization is not only of an economic nature as attested by the outbreak of the H1N1 virus in 2009. With transboundary mobility of persons, goods and information increasing, drug regulations can no longer remain limited to the confines of national boundaries. In this context, diverging national regulations and standards regarding the safety, quality and efficacy of drugs pose various challenges. Requirements and standards vary from state to state, forcing manufacturers to duplicate clinical trials and to file applications for marketing authorization separately in each country. This regulatory heterogeneity is not only a barrier to trade, imposing high costs on the drug developers and manufacturers, but also a hurdle to global health, notably through what has been called the “drug lag”.³⁶

One technique used to meet the international dimension of risk regulation activities has been mutual recognition agreements (MRAs). Premised on the recognition of drug approval standards even in the absence of any harmonization of the respective applicable standards, such agreements with sectoral annexes on pharmaceuticals have been in place between most industrialized countries with stringent regulatory requirements, such as the European Union³⁷, USA³⁸, Japan, Canada, Switzerland or Australia and presuppose the reciprocal recognition of drug approval processes. Characterized by a direct involvement of national agencies in international cooperative schemes,³⁹ these MRAs are a culmination

³⁴ The US Food and Drug Administration points out in a recent report that “Imports of pharmaceutical products have also grown rapidly, at approximately 13% per year, over the past seven years and accounted for more than 350,000 import lines in 2009. This volume accounted for approximately 30% by value of pharmaceutical products used annually [...] Even more than finished medications, the U.S. is increasingly relying on foreign producers for key components. For example, approximately 80% of active ingredients found in pharmaceutical products on U.S. store shelves come from overseas”. See Food and Drug Administration, *PATHWAY TO GLOBAL PRODUCT SAFETY AND QUALITY* (2011) at 15.

³⁵ Frederick M. Abbott & Graham Dukes, *GLOBAL PHARMACEUTICAL POLICY: ENSURING MEDICINES FOR TOMORROW'S WORLD* (Northampton: Edward Elgar, 2009).

³⁶ A “drug lag” is a significant consequence of diverse regulatory requirements that could be defined as the additional time it takes for a country to approve a drug relative to another country or its failure to ever approve a drug approved in another country. It has important implications for public health because it means that new and potentially life-saving medicines are being introduced late and perhaps not introduced at all. See F. Andersson, *The Drug Lag Issue: The Debate Seen From an International Perspective*, 22 *INTERNATIONAL JOURNAL OF HEALTH SERVICES* (1992) 53-72.

³⁷ E.g. *Agreement on Mutual Recognition Between the European Community and the United States of America*, 4th December 2004, *Annex on Pharmaceutical Good Manufacturing Practices*; Australia (OJ L229 on 17/08/1998); Canada: *Sectoral Annex on Good Manufacturing Practice* (OJ L280 on 16/10/1998). Japan (OJ L284 on 29/10/2001). New Zealand (OJ L229 on 17/08/1998) and Switzerland (OJ L114 on 30/04/2002 amended OJ L68 on 12/03/2003).

³⁸ See, among others, MRAs or other cooperative arrangements with Australia (10/11/2000); Canada and Mexico (10/30/1995). All FDA Agreements available at <http://www.fda.gov/InternationalPrograms/Agreement/>

³⁹ The complex web of formal and informal arrangements between these agencies has been described by some scholars as the rise of a so-called “technical diplomacy”. See Linda Horton, *Mutual Recognition Agreements and Harmonization*, 29 *SETON HALL LAW REVIEW* (1998) 692-735.

of an extensive dialogue between peer agencies and usually turn on conformity assessment systems or the exchange of data regarding drug testing results.

However, this technique is not the most efficient way to meet the challenge of globalization. To start with, MRAs can only take place between countries with similar regulatory requirements and administrative cultures – which accounts for the fact that they are mostly limited to the industrialized world.⁴⁰ Another concern is that agreements are often difficult to negotiate as it can take many years for national drug regulatory authorities to find a mutually acceptable regime. These reasons explain why internationally harmonized standards have been dominating on the scene of drug regulations. We now turn to an investigation of different regimes which originate the most important of those standards.

II. Global Drug Safety: A Fragmented World of Standards and Regimes

To face the challenge of globalization and the rapidly changing environment of drug safety, national regulatory agencies engage in close collaboration with their foreign counterparts. This horizontal interagency cooperation between national administrative bodies takes various forms, including participation in various *global forums* for regulatory harmonization and direct collaboration through MRAs and result in a complex transnational regime for drug safety involving both regulatory coordination and regulatory harmonization. Coexistence of multiple transnational regimes is therefore a central feature of medicines quality control. Although there is a genuine functional need to which the emergence of multiple coordination and harmonization regimes is a pragmatic response, those regimes seem to call into question several basic paradigms of regulatory philosophy of the modernist conception of law. For one thing, there seems to be no formal coordination among different regulatory initiatives, which means that a coherent system of regulation seems unlikely to emerge.⁴¹ Such a regulatory chaos may even give rise to the need “to harmonize harmonization”.⁴² Another consequence is what has been aptly called “an erosion of the countries’ authorities”.⁴³ To the extent that pharmaceutical standard-setting is no longer the exclusive province of public authorities, traditional national regulatory structures can claim no monopoly on the rules effectively governing pharmaceuticals drugs.

An overview of the various actors involved in standard-setting activities seems to be in order to illustrate the above points. These actors cover a wide range of entities, from intergovernmental organizations and networks (A) to private and hybrid public-private entities (B).

⁴⁰ It could be said that MRAs require the same level of health protection in both parties and accommodate, rather than suppress regulatory diversity. See Kalypso Nicolaidis & Greg Shaffer, *Transnational Mutual Recognition Regimes: Governance without Global Government*, 68 *LAW AND CONTEMPORARY PROBLEMS* (2005) 268.

⁴¹ Romi Singh, *Harmonizing Harmonization: a Better Map for the Global Regulatory Landscape*, 1 *SCIENTIFIC AMERICAN WORLDVIEW* (2011) at 26 (noting that “as the need for harmonization grow, so do the number of organizations involved” and that “these dozens of harmonization efforts work independently, rather than coordinating their agendas or even communicating with each other.”).

⁴² *Id.* at 25.

⁴³ Kai Peter Purnhagen, *The Challenge of Globalization in Pharmaceutical Law – Is an International Drug Approval System Modeled after the European System Worth Considering?*, 63 *FOOD AND DRUG LAW JOURNAL* (2008) at 623.

A. Inter- and Transgovernmental Regimes

1. The World Health Organization

Relying on its constitutional power in the area of harmonization, the WHO has engaged in standard-making relating to the development, production, quality assurance and surveillance of health products since its creation.⁴⁴ The WHO activities in this area have, however, varied throughout the history of the organization.⁴⁵ In the early stages of its development the WHO tried to address the issue of quality, safety and efficacy for all medicines. Several innovative guidelines were prepared at that time.⁴⁶ However, the focus has progressively moved towards meeting the needs of developing countries, especially in the area of quality of Essential Medicines.⁴⁷ In fact, many global players are relying on WHO's work in this field, ranging from United Nations agencies to global health public-private partnerships and large donors such as the Bill and Melinda Gates Foundation or the Clinton Health Access Initiative, as well as many member states, in order to ensure the quality, safety and efficacy of their procurement of medicines activities.

The WHO work on pharmaceuticals is primarily guided by the WHO medicines strategy, the one currently in force being the WHO Medicines Strategy 2008-2013. The latter, adopted by the World Health Assembly in 2008, places a special emphasis on “[f]ulfilling constitutional obligations to develop norms and standards for pharmaceuticals and biologicals”⁴⁸, highlights how this regulatory function is carried out by the WHO, and states the broad objectives that the WHO should pursue in the interest of access to medicines worldwide.

Several WHO regulatory initiatives are worthy of notice. One of the most important among those initiatives is the adoption of the International Pharmacopoeia⁴⁹ in 1948, which put together all monographs of marketed drugs in collaboration with all stakeholders, including non-governmental organizations. The WHO Expert Committee on Specifications for Pharmaceutical Preparations regularly extends and updates the International Pharmacopoeia.

⁴⁴ On the role of the WHO in the pharmaceutical field, see Lembit Rägo, *Global Disequilibrium of Quality*, in R. Prince (ed.), *PHARMACEUTICAL QUALITY* (Davis Healthcare International Publishing, 2004) 3-21; Gian Luca Burci & Charles-Henry Vignes, *THE WORLD HEALTH ORGANIZATION* (The Hague: Kluwer Law International, 2004) at 131. The WHO standard-setting power regarding the pharmaceuticals is set forth in Articles 2 (“*In order to achieve its objective, the functions of the Organization shall be: u) to develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products...*”) and 21 of the WHO Constitution (“*The Health Assembly shall have authority to adopt regulations concerning: [...] (d) standards with respect to the safety, purity and potency of biological, pharmaceutical and similar products moving in international commerce...*”).

⁴⁵ Ellen N. Cone, *International Regulation of Pharmaceuticals: the Role of the World Health Organization*, 23 *VIRGINIA JOURNAL OF INTERNATIONAL LAW* (1983) at 360-361. It is worth noting that, in the 1980s, the WHO, following the adoption of the Code for the Marketing of Breastmilk Substitutes, did consider adopting a similar code in the field of pharmaceuticals. This project was abandoned due to a fierce reluctance of the industry in industrialized countries. See Molinda Schoepe, *International Regulation of Pharmaceuticals: A WHO International Code of Conduct for the Marketing of Pharmaceuticals?*, 11 *SYRACUSE JOURNAL OF INTERNATIONAL LAW AND COMMERCE* (1984) at 121.

⁴⁶ E.g., WHO, *Principles for Pre-Clinical Trial Testing of Drug Safety* (WHO Technical Report Series No 341, 1966).

⁴⁷ Juhana E. Idänpään-Heikkilä, *Pharmaceutical Products: the International Harmonization and Collaboration Perspectives*, 1 *PHARMACEUTICALS POLICY AND LAW* 25 (1999) at 30-35.

⁴⁸ WHO, *Continuity and Change – Implementing the third WHO Medicines Strategy 2008-2013*, (Geneva, WHO ed., 2010).

⁴⁹ A Pharmacopoeia has been defined as “*an official (legally binding) publication containing recommended quality specifications for the analysis and determination of drug substances, specific dosage forms, excipients and finished drug products*”. See Sabine Kopp & Lembit Rägo, *The International Pharmacopoeia in the Changing Environment*, 9 *PHARMACEUTICAL POLICY AND LAW* 357 (2007) at 360.

Another important initiative is the Manual for drug regulatory authorities, which sets forth prerequisites and operational guidelines for regulatory control exercised by national drug authorities. This Manual is particularly popular among the regulatory authorities of developing countries.⁵⁰

The WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce also deserves a special mention. It aims to provide a series of normative guidelines in order to facilitate the exchange of information between drug regulatory authorities in importing and exporting countries and contains information on the regulatory status of a product and the manufacturer's compliance with the WHO Good manufacturing practice. More than 140 regulatory authorities are among the users of the WHO Certification Scheme.⁵¹

Finally, mention should be made of the WHO Prequalification of Medicines Program launched in 2001 in view of its important contribution to the practical enforcement of the WHO standards in connection with medicines for three high burden diseases, HIV/AIDS, tuberculosis and malaria.⁵² Despite its limited scope of application, the WHO Prequalification Program is one of the most mature international approval schemes for drugs. Its actions consist mainly of the quality verification of relevant medicinal products based upon the WHO guidelines and bioequivalence standards.⁵³ The Program is primarily used by the United Nations agencies, including UNAIDS and UNICEF, as well as public-private partnerships such as the Global Fund Fight AIDS, Tuberculosis and Malaria, and UNITAID to govern procurement choices.⁵⁴

2. The International Conference of Drug Regulatory Authorities (ICDRA)

The International Conference of Drug Regulatory Authorities (ICDRA) is a global forum created under the auspices of the WHO in 1980. The ICDRA is one of the principal tools of cooperation between agencies at the multilateral level. Since its inception, the ICDRA has been a unique forum within which national drug regulatory authorities from amongst the 194 WHO member states with different levels of economic and technological development discuss current issues, exchange points of view and draw up recommendations. Thus, the ICDRA offers an unparalleled opportunity to promote cooperation between developed and developing countries in the field of pharmaceuticals. The ICDRA's recommendations are highly influential and notably promote transparency of safety regulations, regional harmonization initiatives and participation of the civil society (more specifically, association of patients to the standardization processes).

⁵⁰ E.g., Rågo *supra* note 44, at 12.

⁵¹ See Idänpään-Heikkilä, *supra* note 47, at 28.

⁵² E.g., WHO, *Prequalification of Medicines by WHO*, Fact sheet no 278, August 2010.

⁵³ T. G. Dekker, A. J. Van Zyl & O. Gross, *Ongoing Monitoring of Antiretroviral products as part of WHO's Prequalification Programme*, 3 JOURNAL OF GENERIC MEDICINES 96 (2006) at 105. See also, WHO, *WHO and Its Prequalification Programme: an Overview*, 2 WHO PHARMACEUTICALS NEWSLETTER (2005).

⁵⁴ See Dekker, Van Zyl & Gross, *supra* note 53 at 107.

3. Regional Harmonization Initiatives

Although they take part in the WHO initiatives, developing countries also pursue their own harmonization efforts at the regional level, in particular, through the Association of South-East Asian Nations (ASEAN)⁵⁵, the Andean Community, the Harmonization Center within the Asia-Pacific Economic Cooperation (APEC), the Gulf Cooperation Council (GCC), the Pan American Network on Drug Regulatory Harmonization (PANDRH), the South African Development Community (SADC), and the African Medicines Registration Harmonization (AMRH).

These initiatives have resulted in a series of measures ranging from the definition of common technical requirements for drug approval to the streamlining of administrative processes of drug approval. For example, the GCC has developed a centralized registration process based on its own harmonized standards.⁵⁶ The PANDRH promotes harmonization in the Americas through cooperation and adoption of harmonized guidelines.⁵⁷ The AMRH, which gathers regulators from African regional economic communities⁵⁸ through a public-private consortium⁵⁹, seeks to enhance the regulatory capacity of national drug authorities by fostering “cross-country standardization, communication and collaboration”.⁶⁰

These harmonization initiatives aim to pool expertise and to strengthen the institutional and substantive regulatory capacities. The regionalization of standard-setting also provides an opportunity to adapt global standards to the specific needs of a particular region.⁶¹

4. The International Pharmaceutical Inspection Convention / Scheme (PIC/S)

Another harmonization scheme was initiated with the adoption in October 1970 of the Pharmaceutical Inspection Convention (PIC), an international treaty dedicated to the mutual recognition of inspections conducted in other countries. Because it was impossible for the members of the EU to individually become parties to the Convention, a more informal “Pharmaceutical inspection Scheme” was created in 1995, in parallel to the treaty regime. Now referred as PIC/S, this informal cooperative regulatory arrangement between regulatory authorities gather 40 regulatory agencies, including the FDA

⁵⁵ Members of ASEAN are Brunei Darussalam, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam. See Mohd Zin Che Awang, *Regional Harmonization Initiatives – The Association of South-East Asian Nations (ASEAN)*, in PROCEEDINGS OF THE TENTH INTERNATIONAL CONFERENCE OF DRUG REGULATORY AUTHORITIES (ICDRA) (Hong Kong, China, 24-27 June 2002) 53, at 53-4; ASEAN, “ACCSQ Pharmaceutical Product Working Group” <<http://www.aseansec.org/14903.htm>>

⁵⁶ Laïla A. Rahman, *Centralized Drug Registration System in the Gulf Region*, in PROCEEDINGS OF THE TENTH INTERNATIONAL CONFERENCE OF DRUG REGULATORY AUTHORITIES (ICDRA), (Hong Kong, China, 24-27 June 2002) at 56.

⁵⁷ PANDRH, *Pan American Network for Drug Regulatory Harmonization (Norms and Regulations)*, <<http://www.paho.org/English/AD/THS/EV/Norms-pandrh.pdf>>.

⁵⁸ AMU - Arab Maghreb Union, CEMAC: Monetary Community of Central Africa, COMESA: The Common Market for Eastern and Southern Africa, EAC: The East African Community, ECCAS: Economic Community of Central African States, ECOWAS: The Economic Community of West African States, ECSA: East, Central and Southern African Health Community, IGAD: The Intergovernmental Authority on Development, OCEAC: The Organization for the Coordination and Cooperation for the fight against Endemic Diseases in Central Africa, SADC: Southern African Development Community, UEMOA: The Economic and Monetary Union of West Africa, WAHO: The West African Health Organization.

⁵⁹ This public-private consortium is composed of the WHO, the African Union Commission, the Pan African Parliament, the New Partnership for Africa’s Development, The Bill and Melinda Gates Foundation, the Clinton Foundation Health Access Initiatives and the UK Department for International Development. See AMRH Website, www.amrh.org

⁶⁰ See AMRH, *Concept Paper: Harmonizing Drug Registration in Africa*, December 2008, at 2.

⁶¹ Most of these regional initiatives participate in the Global Cooperation group of the ICH. See *infra*. p. 15.

since 2011, to harmonize inspection systems and achieve the mutual recognition of inspections worldwide. The PIC/S aims to harmonize inspection procedures at the global level by elaborating common good manufacturing practice standards. Participation in this informal arrangement is premised on the similarity of the level of risk regulation applied by the applicant agency. As the PIC/S operates as a network of peers, the accession mechanism implies a review by standing members to assess whether the applying authority is able to apply an inspection system comparable to that of current PIC/S authorities. The PIC/S works closely with the WHO and the ICH. Notably, with regard to the latter, PIC/S has been instrumental in drafting some of the ICH guidelines, such as the ICH guidelines on active pharmaceutical ingredients.

B. Transnational Regimes: Private actors as ‘Global Standardizers’

1. The Council for International Organizations of Medical Sciences (CIOMS)

The Council for International Organizations of Medical Sciences (CIOMS) is an international nongovernmental organization founded under the auspices of the WHO and the UNESCO in 1949. Composed of 48 International Scientific Associations such as the World Medical Association and 18 National Medical Associations, CIOMS represents a significant proportion of the biomedical scientific community.⁶² Although the CIOMS’s major focus is on bioethics issues, the CIOMS launched in the early 1980s a “Drug Development and Use” program. Since then the CIOMS has issued numerous recommendations with regard to pharmaceuticals⁶³, notably to provide guidance on the assessment and monitoring of adverse drug reaction.⁶⁴ Its work and guidelines on pharmacovigilance have largely influenced other harmonization initiatives such as the ICH.⁶⁵

2. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

Often described as a paradigmatic case of informal international law-making and a hybrid public-private standard-setting body at the international level⁶⁶, the ICH was set up in 1990 with the objective of harmonization of drug regulations in high-standards countries⁶⁷ - namely, Europe (through the European

⁶² See http://www.cioms.ch/about/membership/frame_membership.htm

⁶³ These recommendations concern, among other things, international reporting of adverse drug reactions, and periodic drug-safety updates, core clinical safety information on drugs, evaluation of benefit/risk balance, current challenges of pharmacovigilance, management of safety information from clinical trials and development safety update report (DSUR) and signal detection in pharmacovigilance.

⁶⁴ CIOMS, *Current Challenges in Pharmacovigilance: Pragmatic Approaches*, CIOMS V (2001).

⁶⁵ According to some authors, the CIOMS was used as a think tank by international experts in order to gain consensus on the very concept of pharmacovigilance planning. See David Demortain, *SCIENTISTS AND THE REGULATION OF RISKS: STANDARDISING CONTROL* (Northampton, Edward Elgar, 2011) at 102.

⁶⁶ See Ayelet Berman, *The Role of Domestic Administrative Law in the Accountability of Transnational Regulatory Networks: The Case of the ICH*, IRPA Global Administrative Law Working Paper 2012/1, 2012.

⁶⁷ Richard B. Arnold, *Objective and Preparation of the Conference and the Role of the Workshops*, in P. F. D’Arcy & D. W.G. Harron (ed.) *THE FIRST INTERNATIONAL CONFERENCES ON HARMONIZATION BRUSSELS 1991* (Belfast: The Queen’s University, 1992) (discussing that “today, concerns about healthcare costs, including drug and drug development costs, the emergence of new disease problems, ethical concerns about the use of experimental animals and possibly unnecessary procedures in humans provide a powerful incentive to rationalize technical requirements for drug registration”).

Medicines Agency), the USA (through the Food and Drug Administration), and Japan (through the Pharmaceuticals and Medical Devices Agency). In this sense, ICH is a unique forum gathering regulatory agencies from the three regions along with their pharmaceutical industry associations (European Federation of Pharmaceutical Industries and Associations - EFPIA, The Pharmaceutical Research and Manufacturers of America - PhRMA, and Japan Pharmaceutical Manufacturers Association - JPMA).⁶⁸ It also includes observers such as the WHO, Health Canada and the European Free Trade Association (EFTA) represented by Swissmedic, the Swiss drug regulatory authority. This restricted membership policy is indicative of the nature of the ICH, which is a “club” of countries sharing similar levels of health protection and the same interests as regards the pharmaceutical markets.⁶⁹

This highly institutionalized body is based on a constitutional act embedded in “Terms of Reference”⁷⁰ and is governed by a Steering Committee consisting of founding members with voting rights and other interested parties invited on an ad hoc basis. The International Federation of Pharmaceuticals Manufacturers and Associations (IFPMA) hosts the ICH Secretariat and participates as a non-voting member of the Steering Committee. The Steering Committee determines which interested parties affected by the outcomes of the ICH’s work may be allowed to participate in the work of the ICH.

The 50 harmonized guidelines adopted by the ICH define the scientific requirements that apply within the context of the drug approval in terms of quality, safety and efficacy.⁷¹ These guidelines are implemented in the three participating regions as guidance documents.⁷² Among the major achievements has been the Common Technical Document (CTD) (agreed in 2000), which provides for a harmonized structure and format for new product applications, avoiding the need to generate different registration dossiers. Specifications for new drug substances and products were agreed (1999) to improve the situation where conflicting standards were laid down for the same product in different regions, leading to increased expenses and risks of error as well as a potential cause for interruption of product supply. Another achievement to note is the Guideline for Good Clinical Practice (GCP) (1996), an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.⁷³ This provides a unified standard for the three regions to facilitate the mutual acceptance of clinical data by the regulatory authorities.

⁶⁸ Yves Juillet, *Internationalisation of Regulatory Requirements*, 9 PHARMACEUTICALS POLICY AND LAW (2007) 369, at 371.

⁶⁹ Rosemarie Kanusky, *Pharmaceutical Harmonization: Standardizing Regulations among the United States, the European Economic Community, and Japan*, 16 HOUSTON JOURNAL OF INTERNATIONAL LAW (1994) 665-707.

⁷⁰ See *Revised Terms of Reference*, in ICH, THE VALUE AND BENEFITS OF ICH TO DRUG REGULATORY AUTHORITIES – ADVANCING HARMONIZATION FOR BETTER HEALTH (2010) at 17.

⁷¹ See Sarah Branch, *Guidelines from the International Conference on Harmonisation (ICH)*, 38 JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS (2005) 798-805.

⁷² According to the FDA, guidance documents are “documents prepared for FDA staff, applicants/sponsors, and the public that describe the interpretation of or policy on a regulatory issue” (21 CFR 10.115). In the US, these guidelines are published in the Federal Register and made available on the FDA website. See Paul M. Booth, *FDA Implementation of Standards Developed by the International Conference on Harmonisation*, 52 FOOD AND LAW JOURNAL (1997) 203. In Europe, the guidelines are published by the European Commission in Volume III of the *Rules Governing Medicinal Products in the European Union* after being adopted by the European Committee for Medicinal Products for Human Use (CHMP). As such, ICH guidelines gain “the same status as other European scientific guidelines and replace existing guidelines on the subject covered”. See EMEA, *Procedure for European Union Guidelines and Related Documents with the Pharmaceutical Legislative Framework* (2005) at 4.

⁷³ Sarah Bahir, *An International Legal System Regulating the Trade in the Pharmaceutical Sector and Services Provided by Human Subjects*, 6 ASPER REVIEW OF INTERNATIONAL BUSINESS AND TRADE LAW (2006) 157-175.

Although the ICH was originally intended to be a limited initiative, it has extensively broadened its activities towards non-ICH countries and is expected to become a genuine global player in standard-setting in the field of safety, quality, efficacy and other guidelines related to medicinal products. The establishment of the Global Cooperation Group (GCG) within the Steering Committee in 1999 constitutes a crucial move towards this end. Initially composed of members of the Steering Committee, observers and any *ad hoc* interested party, the GCG was expanded in 2004, at the Osaka Conference where new GCG terms of reference were adopted, to include many of the Regional Harmonization Initiatives (composed, as mentioned above, mostly of developing countries). Six non-ICH regions developing certain regional harmonization activities are participating in the GCG, namely APEC, ASEAN, GCC, PANDRH, SADC and, from June 2011, EAC (East African Community). In 2008, the GCG was even expanded to individual drug authorities from non-ICH Countries, including “pharmerging”⁷⁴ countries such as China, India, Brazil or Russia.

Officially, the goal of this group is to share information with, and provide training to non-ICH countries on the ICH standards.⁷⁵ The actual target of the GCG seems to be the expansion of the use of ICH guidelines to non-ICH countries.⁷⁶ Coupled with a recognition of a more proactive role to regulators from developing countries, the GCG could indeed ultimately contribute to the perception of the ICH as a global pharmaceutical standard-setting body.⁷⁷

III. Global Pharmaceutical Standards as Evidence of the Transformation of Regulatory Paradigms

Pharmaceutical standards produced by the regimes described above display many characteristics which are usually taken as substantiating the claim that standards radically depart from the logic of the traditional regulatory paradigm at the international level. In this part I will take up some of these characteristics and set out to examine to what extent they support the radical transformation thesis.

A. Pharmaceutical Standards: Rules of Conduct or Mere Scientific Facts?

As stated in the introduction, pharmaceutical standards rely on a significant amount of technical and scientific expertise.⁷⁸ This feature of standards is frequently contrasted with what legal rules are

⁷⁴ Raymond Hill & Mandy Chui, *The Pharmerging Future*, 29 IMS HEALTH (2009). See also IMS Health, *Pharmerging Shake-Up: New Imperatives in a Redefined World*, 2010 (predicting that 17 pharmerging countries will in aggregate expand by US\$90 billion during 2009-13 and contribute 48 percent of annual market growth in 2013). These countries are the followings: China, Brazil, Russia, India, Venezuela, Poland, Argentina, Turkey, Mexico, Vietnam, South Africa, Thailand, Indonesia, Romania, Egypt, Pakistan, and Ukraine.

⁷⁵ According to its mission statement, the GCG aims “To promote a mutual understanding of regional initiatives in order to facilitate harmonization processes related to ICH guidelines regionally and globally and to strengthen the capacity of drug regulatory authorities to utilize them”. See ICH, Global Cooperation Group, *Strategy on Training and Capacity-building Related to the Use of ICH Guidelines*, 2010, available at www.ich.org

⁷⁶ Karin Timmersman, *Harmonization, Regulation, and Trade: Interactions in the Pharmaceutical Field*, 34 INTERNATIONAL JOURNAL OF HEALTH SERVICES (2004), 643, at 655 (pointing out that it is clear that the GCG is intended to “position the ICH guidelines as the international norm.”).

⁷⁷ See Mike Ward, *The Global Cooperation Group – A Bridge from ICH to the World Beyond*, in *The Value and Benefits of ICH to Drug Regulatory Authorities – Advancing Harmonization for Better Health* (ICH, 2010). (emphasizing that “GCG efforts have evolved from simply information sharing to active dialogue to the current results-oriented action.”).

⁷⁸ See, among others, Bengt Jacobsson, *Standardization and Expert Knowledge*, in Nils Brunsson & Bengt Jacobsson (eds.), *A WORLD OF STANDARDS* (Oxford: Oxford University Press, 2000) at 40-49; Karl-Heinz Ladeur, *The Integration of Scientific*

traditionally taken to be.⁷⁹ The contrast is usually built along the following lines. Validity of standards rests mainly on their according with the world of facts. To use a kelsenian term⁸⁰, a standard is a matter of “*sein*” (is), even though it formally takes the form of “*sollen*” (ought): a standard should be followed inasmuch as it rightly describes a factual phenomenon as a matter of science. By contrast, a legal rule is a matter of “*sollen*”. It must be followed not because it corresponds to a fact as a matter of science, but because it has been set forth following a predetermined procedure and by specific institutions which have been empowered to enact the rule in question.

Although very tempting, this distinction needs to be strongly qualified. The fact that standards are backed up by scientific knowledge and expertise does not mean that they are objective, nor does it mean that they operate as laws of physics. No actor is forced to follow a standard in the same sense as we are *volens nolens* subject to the laws of physics. A standard is followed because of a conscious decision and because it responds to certain value-laden needs.⁸¹ To take the example of pharmaceutical standards, these standards are followed because protection of public health is a much cherished value in our societies. Moreover, as we will see later, standard-making involves a clash between different interests and therefore, often requires giving priority to some of those interests over others, just in the same way as in the case of legal rules.

B. Compliance with International Pharmaceutical Standards: Beyond the Binding / Non-Binding Dichotomy

Pharmaceutical standards do not fit into the traditional taxonomy of sources of international law. More generally, traditional law’s binary logic of *binding v. non-binding* can hardly account for those standards. Although standards are purely voluntary as a matter of law, they enjoy a remarkable level of efficacy. What has been called “a formidable puzzle”,⁸² namely a general inquiry as to why voluntary standards are followed and are by and large successful in impacting the behavior of their targets is also relevant in the context of pharmaceutical standards. Several lines of inquiry have been followed in answering this question and they all seem relevant with regard to these standards.

For instance, it has been suggested that the very fact that standards are both flexible and voluntary can explain their success as they can be adapted, if need be, to a given circumstance by users.⁸³ Being voluntary, standards can also be more easily revised in light of the scientific and technological changes.⁸⁴

and Technological Expertise into the Process of Standard Setting According to German Law, in Christian Joerges, Karl-Heinz Ladeur & Ellen Vos (eds.), *INTEGRATING SCIENTIFIC EXPERTISE INTO REGULATORY DECISION MAKING* (Baden-Baden, Nomos, 1997) at 77-100.

⁷⁹ Paul Amselek, *Norme et loi*, 25 *ARCHIVES DE PHILOSOPHIE DU DROIT* (1989) at 89. See also Simon Charbonneau, *Norme juridique et norme technique*, 28 *ARCHIVES DE PHILOSOPHIE DU DROIT* (1983) at 285.

⁸⁰ Hans Kelsen, *GENERAL THEORY OF LAW AND STATE* (Cambridge, Mass. Harvard University Press, 1949) at 45-6.

⁸¹ This is for instance clearly exemplified in the ISO/IEC Guide which states that standards aim “at the promotion of optimum community benefits.” (ISO/IEC Guide 2:2004, definition 3.2).

⁸² See Arts & Kerwer, *supra* note 18, at 144.

⁸³ Kenneth W. Abbott & Duncan Snidal, *International ‘Standards’ and International Governance*, 8 *JOURNAL OF EUROPEAN PUBLIC POLICY* 345 (2001) at 355-356.

⁸⁴ Isabelle Vacarie & Alain Supiot, *Santé, sécurité et libre-circulation des marchandises – règles juridiques et normes techniques*, 18 *DROIT SOCIAL* (1993) at 22.

It has also been pointed out that voluntary nature of standards is more considerate of national sovereignties and contributes to their wide-spread use by public authorities.⁸⁵

Another factor which has been emphasized is the scientific expertise which backs up standards.⁸⁶ Given the authority that science enjoys in modern societies, such expertise enhances the legitimacy of standards, and promotes the compliance with the latter, the legitimacy being an important “compliance pool” as famously observed by Thomas Franck.⁸⁷

The question as to what extent these features are novelties at the international level cannot be provided a single-sentence answer. What I would like to emphasize is the fact that at least some of the explanations described above are not totally unknown in international legal experience. Let us take for instance the explanation based upon the voluntariness and flexibility of standards. As readers familiar with the discussions about “soft law” in international law can easily recognize, this is one of the explanations which have been traditionally provided as to the rise of “soft law” at the global level. The most significant early manifestations of “soft law” have been in the areas of international cooperation which are subject to rapidly changing circumstances such as monetary policies or exploration of outer space. Under such conditions, traditional techniques of international law-making could not meet pressing needs for regulation. “Soft law” emerged to satisfy such functional needs.

One could be tempted to think that the fact that compliance with pharmaceutical standards has much to do with the authority of scientific knowledge is not an experience previously known at the international level. Although the significance of science is indisputably more pronounced in case of pharmaceutical standards, one should, however, not overlook the fact that there is nothing truly new about the authority that expertise enjoys. Expertise is consistently accompanied in modern societies by what has been called “deference to cognitive authorities”.⁸⁸ As the sociologist Edward Shils points out, such deference is one of the constant features of human interaction. The deference to which an actor is entitled is a function of the sort of things valued by a given society. According to Shils, “the disposition to defer and the performance of acts of deference are evoked by the perception, in the person or classes of persons perceived, of certain characteristics or properties of their roles or actions”.⁸⁹ Shils calls these characteristics or properties “deference-entitling property”.⁹⁰

A good illustration of how such deference-entitling properties work at the level of more traditional international law is the legal authority of pronouncements of UN’s human rights treaty-bodies. Even though they are, technically speaking, not binding, the General Comments of the Human Rights

⁸⁵ Dieter Kerwer, *Rules that Many Use: Standards and Global Regulation*, 18 GOVERNANCE (2005) at 616.

⁸⁶ Bengt Jacobsson, *Standardization and Expert Knowledge*, in A WORLD OF STANDARDS, *supra* note 78, at 40.

⁸⁷ Thomas M. Franck, *Legitimacy in the International System*, 82 AMERICAN JOURNAL OF INTERNATIONAL LAW (1988) at 706.

⁸⁸ Stephen Stich & Richard Nisbett, *Expertise, Justification, and the Psychology of Inductive Reasoning*, in Thomas L. Haskell (ed.), THE AUTHORITY OF EXPERTS: STUDIES IN HISTORY AND THEORY (Bloomington: Indiana University Press, 1984), 226 at 236-237 (pointing out that “it is a hallmark of an educated and reflective person that he recognizes, consults, and defers to authority on a wide range of topics. ... Few educated laypersons would consider questioning the consensus of authorities on the authenticity of a painting, the cause of an airline crash, or the validity of a new theorem. Indeed, it is our suspicion that one of the principle effects of education is to socialize people to defer to cognitive authorities.”). See also, Jeffery Atik, *Science and International Regulatory Convergence*, 17 NORTHWESTERN JOURNAL OF INTERNATIONAL LAW AND BUSINESS (1996-7) at 738 (“Science, more than religion, more than traditional ways, is unassailable within its domain.”).

⁸⁹ Edward Shils, CENTER AND PERIPHERY. ESSAYS IN MACROSOCIOLOGY (Chicago: University of Chicago Press, 1982), at 145.

⁹⁰ *Id.* at 147.

Committee (HRC) or the Committee on Economic, Social and Cultural Rights enjoy a significant degree of authority precisely because those comments are generated by expert bodies composed of specialists of human rights.⁹¹ As Bruno Simma⁹² points out, it is no argument to reject a General Comment of the HRC on the ground that a general comment is not technically binding when one realizes that general comments are reasoned interpretations of the Covenant by the very expert body set up by the Covenant.

There are also other reasons for thinking that all is not new under the sun of compliance with pharmaceutical standards. A special mention must be made in this regard of what has been called “third-party endorsement”.⁹³ Standards can be transformed into mandatory directives by being incorporated into legally binding rules. ICH and WHO guidelines are in fact extensively incorporated in domestic laws and are mandatory as a matter of “hard law”.⁹⁴ WTO law provides another illustration of this technique. According to the WTO Agreement on Technical Barriers to Trade (TBT), which applies to pharmaceutical regulations⁹⁵, whenever a technical regulation pursues a legitimate objective and “is in accordance with relevant international standards, it shall be ... presumed not to create an unnecessary obstacle to international trade”.⁹⁶ It is true that the presumption of conformity recognized in the TBT is not conclusive and can be defeated in theory.⁹⁷ It is also true that states are not legally obligated to follow the standards in question. According to the TBT Agreement, members can decide not to observe those standards if they consider that “such international standards or relevant parts would be an ineffective or

⁹¹ It is, for instance, remarkable that such a traditional public international law institution as the ICJ has relied on the views and general comments of the Human Rights Committee without even raising any question as to their legal force. See *Legal Consequences of the Construction of a Wall in the Occupied Palestinian Territory*, Advisory Opinion of 9 July 2004, ICJ Reports 2004, p. 179, para. 109; *Ahmadou Sadio Diallo (Republic of Guinea v. Democratic Republic of the Congo)*, Judgment of 30 November 2010, paras 66, 77. A *dictum* in the latter case also supports the position defended here: “Although the Court is in no way obliged, in the exercise of its judicial functions, to model its own interpretation of the Covenant on that of the Committee, it believes that it should ascribe great weight to the interpretation adopted by this independent body that was established specifically to supervise the application of that treaty.” (para. 66).

⁹² Bruno Simma, *Commissions and Treaty Bodies of the UN System: Comment*, in Rüdiger Wolfrum & Volker Röben (eds.), *DEVELOPMENTS OF INTERNATIONAL LAW IN TREATY MAKING* (Berlin: Springer, 2005) at 585 (“I would venture to say that to a practitioner in a foreign office or ministry of justice it will not make that much of a difference whether an international pronouncement on what to do or not to do in human rights matters originates from Strasbourg, that is, whether it is pronounced by a court, or whether it stems from a human rights treaty body... This will be especially true if the media have an interest in the matter, because then to explain to the press ‘You see, we don’t have to care for what such and such committee in Geneva has said about us because what these people say is not legally binding, whereas if the Strasbourg Court has said the same thing we would have to conform to its views’, may satisfy some lawyers but hopefully not the press and the public ... Thus, the chances are quite good that corrective action of the same intensity will be taken in both cases”).

⁹³ Arts and Kewer, *supra* note 18, at 146.

⁹⁴ WHO guidelines are, for instance, incorporated into the domestic legislations of certain developing countries. This is the case in the recent Brazilian legislation on drug regulation. See, for instance, Resolution - RDC n° 25 issued on December 9, 1999 that refers directly to “[t]he recommendation of the World Health Organization (WHO) concerning the Quality Certification of Pharmaceutical Products for International Trade”. With regard to ICH members see *supra* note 72.

⁹⁵ Mary H. Eliason, *Regulatory Marketing Approval for Pharmaceuticals as a Non-Tariff Barrier to Trade: Analysis Under the WTO’s Agreement on Technical Barriers to Trade*, 8 SAN DIEGO INTERNATIONAL LAW JOURNAL (2006-7) at 559.

⁹⁶ The WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS) follows the same logic and provides that “sanitary or phytosanitary measures which conform to international standards, guidelines or recommendations shall be deemed to be necessary to protect human, animal or plant life or health, and presumed to be consistent with the relevant provisions of this Agreement and of GATT 1994” (article 3.2).

⁹⁷ This is why the technique in question has been qualified as “soft incorporation” (Joost Pauwelyn, *CONFLICT OF NORMS IN PUBLIC INTERNATIONAL LAW: HOW WTO LAW RELATES TO OTHER RULES OF INTERNATIONAL LAW* (Cambridge: Cambridge University Press, 2003) at 350).

inappropriate means for the fulfillment of the legitimate objectives pursued”.⁹⁸ It is clear, however, that analysis of the legal effects of global pharmaceutical standards cannot be confined to these formal considerations. First of all, even though the presumption of conformity, which is attached to measures consistent with international standards, can be defeated, this cannot be done easily given the highly technical nature of the matter and the solid scientific justifications which support those standards. Secondly, even though recourse to relevant international standards is not mandatory as a matter of law, non-recourse to such standards brings with it additional obligations: a WTO member who does not observe relevant international standards must provide justification for this. It should, therefore, come as no surprise that in general international standards are so carefully observed that they can arguably be described as “binding in practice”.⁹⁹ It should, however, be noted that the WTO’s technique of incorporation is only available for those of pharmaceutical standards produced by international standard-setting bodies that are open “on a non-discriminatory basis to relevant bodies of at least all WTO Members”¹⁰⁰ – which means that as of now only the standards set forth by the WHO, PIC/S and ICDRA could qualify for the purposes of the incorporation by the WTO.

The above remarks purport to show that compliance with pharmaceutical standards, which is often described as marking a radical transformation of the regulatory logic at the international level can be analogized with more traditional experience that international law has gone through. It may well be the case that in the case of pharmaceutical standards, we are witnessing a phenomenon of a greater magnitude. One should not, however, lose sight of the fact that what has been part of legal experience is also at work here.

C. Legitimacy Deficit or Alternative Grounds of Legitimacy?

Although the issue of legitimacy has been described as “one of the central questions – perhaps the central question – in contemporary world politics”¹⁰¹, legitimacy remains a frequently employed, but rarely clearly defined notion which runs a considerable risk of confusion when used with insufficient rigor.¹⁰² Such a risk is all the more daunting considering the various possible dimensions of legitimacy. As regards pharmaceutical standards, the most frequently voiced legitimacy concern is related to the democratic legitimacy.¹⁰³ Since standard-setting bodies “operate outside the system of democratically

⁹⁸ Likewise, the SPS Agreement recognizes the right of members to “introduce or maintain sanitary or phytosanitary measures which result in a higher level of sanitary or phytosanitary protection than would be achieved by measures based on the relevant international standards, guidelines or recommendations.” (article 3.3).

⁹⁹ Alvarez, *supra* note 2, at 223.

¹⁰⁰ WTO, TBT Committee, *Decision of the Committee on Principles for the Development of International Standards* (2000) 6.

¹⁰¹ Andrew Moravcsik, *Is There a “Democratic Deficit” in World Politics? A Framework for Analysis*, 39 GOVERNMENT AND OPPOSITION (2004) at 336.

¹⁰² For a recent attempt at clarifying the concept of legitimacy and its relevance in law, see Richard H. Fallon, Jr., *Legitimacy and the Constitution*, 118 HARVARD LAW REVIEW 1787 (2005).

¹⁰³ Michael J. Warning, *TRANSNATIONAL PUBLIC GOVERNANCE: NETWORKS, LAW AND LEGITIMACY* (Basingstoke: Palgrave Macmillan, 2009) at 222.

legitimized actors”¹⁰⁴, a regulatory activity carried out by unelected experts and such industry-driven entities as the ICH inevitably and justifiably gives rise to such concerns.

Legitimacy criticisms mounted against the pharmaceutical standards call, however, for a certain amount of clarification. I will examine those criticisms focusing specifically on the ICH both because it has been the most frequent target of such criticisms¹⁰⁵, and because, the standards set forth by the ICH are very influential.

First, it is important to properly assess the merits of legitimacy criticisms from the standpoint of the approach taken in this paper. There is no doubt that the absence of democratic legitimacy is a serious concern. It would, however, be misleading to think that such concerns are met in the traditional areas of international legal regulation.¹⁰⁶ It is, for instance, well known that custom, which is considered to be “at the heart of international law”¹⁰⁷, presents serious shortcomings in terms of legitimacy to the extent that not all states participate in its making on an equal basis¹⁰⁸, not to mention the fact that the process of formation of custom in general is hardly rationalizable. In the same vein, legitimacy of traditional international organizations has been questioned on the ground of the lack of elections, lack of due process, or inequality of influence.¹⁰⁹ It would, therefore, be an oversimplification to think that pharmaceutical standards represent an illegitimate exception in a world of global governance with no legitimacy concerns.

Second, to say that pharmaceutical standards lack democratic legitimacy is not to say that they can claim no legitimacy at all. Richard Fallon’s recent study on legitimacy provides a helpful starting point to understand the kind of legitimacy that pharmaceutical standards may enjoy. Fallon distinguishes three concepts of legitimacy based upon the terms in which legitimacy is discussed: moral, legal and sociological.¹¹⁰ What is interesting for our purposes is the sociological legitimacy that Fallon defines as follows:

“When legitimacy is measured in sociological terms, a ... regime, [an] institution, or official decision possesses legitimacy in a strong sense insofar as the relevant public regards it as justified, appropriate or otherwise deserving of support for reasons beyond fear of sanctions or mere hope for personal reward”.¹¹¹

¹⁰⁴ *Id.*

¹⁰⁵ See, in particular, Stéphanie Dagon, *Global Harmonization Through Public-Private Partnership: The Case of Pharmaceuticals*, IRPA GAL Working Paper, 2012/2.

¹⁰⁶ For an analysis of legitimacy of international law, see Matthias Kumm, *The Legitimacy of International Law: A Constitutionalist Framework of Analysis*, 15 *EUROPEAN JOURNAL OF INTERNATIONAL LAW* (2004) 907; Joseph Weiler, *The Geology of International Law - Governance, Democracy and Legitimacy*, 64 *ZAÖRV* (2004), 547.

¹⁰⁷ Brigitte Stern, *Custom at the Heart of International Law*, 11 *DUKE JOURNAL OF COMPARATIVE & INTERNATIONAL LAW* (2001) 89.

¹⁰⁸ As pointed out by Brigitte Stern, custom “represents the dominant ideology of international society, taken up by all, even though it may be wanted by some and endured by others.” (*Id.*, at 108).

¹⁰⁹ Jonathan G.S. Koppell, *WORLD RULE: ACCOUNTABILITY, LEGITIMACY AND THE DESIGN OF GLOBAL GOVERNANCE* (Chicago: University of Chicago Press, 2010) at 32. See also David Held, *The Transformation of Political Community: Rethinking Democracy in the Context of Globalization*, in Ian Shapiro & Casiano Hacker-Cordon (eds.), *DEMOCRACY’S EDGES* (Cambridge University Press, 1999) at 84-101; Robert Dahl, *Can International Organizations Be Democratic? A Skeptic’s View*, in *DEMOCRACY’S EDGES*, at 19-36; Michael Zurn, *Global Governance and Legitimacy Problems*, 39 *GOVERNMENT AND OPPOSITION* (2004) 260-87.

¹¹⁰ See Fallon, *supra* note 102, at 1794-1801.

¹¹¹ *Id.* at 1795. See also, Michael L. Wells, “*Sociological Legitimacy*” in *Supreme Court Opinions*, 64 *WASHINGTON & LEE LAW REVIEW* (2007) at 1011.

Building on this definition, I propose to approach the legitimacy of pharmaceutical standards as a legitimacy which rests essentially on sociological grounds. Two possible sources of sociological legitimacy are worthy of notice with regard to those standards: procedural and substantive.

1) The first possible source of legitimacy may be sought in the procedure followed in standard-setting organizations. It may be tempting to analogize legitimacy of pharmaceutical standards setting procedures with the kind of procedural legitimacy that many legal systems promote. The latter can be described building on the “procedural paradigm” defined by Jürgen Habermas:

“This paradigm of law, unlike the liberal and social welfare-models, no longer favors a particular ideal of society, a particular vision of the good life, or even a particular political option. It is ‘formal’ in the sense that it merely states the necessary conditions under which legal subjects ... can reach an understanding with one another about what their problems are and how they are to be solved”.¹¹²

This description seems at first sight to correspond to the way in which pharmaceutical standard setting organizations operate to the extent that they exemplify self-regulation: the standards are often set forth by the very same actors that are governed by them, be it pharmaceutical industries or drug regulations authorities. One may be tempted to think that what such an experience exhibits is a supreme form of legitimacy as rules of the game are not imposed from outside, but are negotiated directly by the players themselves. Such an outlook would, however, overlook the fact that most standards affect many actors – from patients to drug authorities of developing countries - that do not meaningfully participate in their production.

Moreover, what Habermas has in mind is the organization of rule-setting activities of non-public structures by *public* authorities. To the extent that public authorities enjoy democratic legitimacy, the legitimacy of rule-setting activities of non-public structures is a sort of indirect legitimacy which is a function of their compliance with procedural rules laid down for the regulation of their rule-setting activities. Thus, instead of setting what substantive outcomes should be in advance, public authorities institutionalize “the procedures and communicative presuppositions” through which substantive outcomes can be reached.¹¹³ The legitimacy of those outcomes reposes exclusively upon the legitimacy of these procedural and communicational conditions.¹¹⁴ This point is clearly made by Gunther Teubner:

“Law's role is to decide about decisions, regulate regulations, and establish structural premises for future decisions in terms of organization, procedure, and competencies. Specific outcomes in other subsystems will be influenced by law's role in setting the parameters for decision making, but they will not be legal mandates, for law would not have determined them”.¹¹⁵

It seems difficult to apply a similar analysis to global pharmaceutical standards, as it can hardly be said that standard-setting procedures in organizations such as the ICH or the CIOMS are set forth by public authorities given the mixed or purely private nature of those organizations. This is, however, not to

¹¹² Jürgen Habermas, *BETWEEN FACTS AND NORMS* (Cambridge, MIT Press, 1996), at 445.

¹¹³ *Id.* at 437.

¹¹⁴ *Id.*

¹¹⁵ Gunther Teubner, *Substantive and Reflexive Elements in Modern Law*, 17 *LAW & SOCIETY REVIEW* 239 (1983) at 275.

say that no such analogy is conceivable at the international level once we keep in mind the specific features of the international setting. A particularly apt illustration is provided in the 2000 Decision of the WTO Committee on Technical Barriers to Trade on Principles for the Development of International Standards, which sets up a certain number of procedural principles to be followed in the elaboration of international standards.¹¹⁶ Particularly important among these in terms of organizing principles are transparency, openness, impartiality and consensus. Admittedly, as the WTO Panel observed in *EC – Sardines*, the TBT Committee’s decision is a statement of preferences rather than a binding document.¹¹⁷ Nonetheless, since many standard-setting organizations are understandably interested in obtaining official recognition from WTO structures, they are likely to observe the guidelines provided by the WTO in an attempt to maximize their potential.¹¹⁸ Such is the case, for instance, with ISO, which in its governing documents refers to the mandatory applicability of the TBT Committee Decision on Principles for the Development of International Standards.¹¹⁹ Similarly, one can find references to the decision of the TBT Committee within bilateral or regional free-trade agreements which expressly provide that international standards prevailing in the relations between the parties are those respecting the principles of the TBT Committee Decision.¹²⁰

It seems that the ICH also seeks recognition by the TBT Committee,¹²¹ although it would be difficult for the ICH – at least if no change is made to its current status - to qualify as a standard-setting organization for purposes of the TBT Agreement, as the ICH does not meet the condition of openness, “on a non-discriminatory basis to relevant bodies of at least all WTO Members”.¹²²

This seems to be one of the most important legitimacy deficits of the ICH as the developing countries do not participate in its standard setting activities.¹²³ Such a complete lack of representation involves a significant risk of “procedural disregard” which has been defined by Professor Richard Stewart as “failure by global regulatory authorities to take into account and give adequate weight in decision-

¹¹⁶ *Decision of the TBT Committee on Principles for the Development of International Standards*, *supra* note 100.

¹¹⁷ WTO, *European Communities – Trade Description of Sardines (EC – Sardines)*, Panel Report, WT/DS231/R, 29 May 2002, para. 7.91.

¹¹⁸ See Steve Charnovitz, *International Standards and the WTO*, George Washington University Law School, Public Law & Legal Theory Research Paper Series, Working Paper No. 133, 2005, p. 9.

¹¹⁹ See the ISO Technical Management Board Policy Statement and Implementation Guide on ‘Global Relevance of ISO Technical Work’ and the ISO Code of Ethics (June 2004). On this, see Eran Shamir-Borer, “The Evolution of Administrative Law-Type Principles, Mechanisms and Practices in the International Organization for Standardization (ISO)”, paper presented at the Viterbo II Global Administrative Law Conference, June 2006, at 23.

¹²⁰ See, e.g., Article 7.3 of the *US-Morocco 2004 Free Trade Agreement*: “In determining whether an international standard, guide, or recommendation within the meaning of Articles 2 and 5 and Annex 3 of the TBT Agreement exists, each Party shall apply the principles set out in *Decisions and Recommendations adopted by the Committee since 1 January 1995*, G/TBT/1/Rev.8, 23 May 2002, Section IX issued by the WTO Committee on Technical Barriers to Trade”.

¹²¹ See Timmersman, *supra* note 76, at 654 (“the ICH standards are set to become the TBT Agreement’s global standards for technical regulations related to pharmaceuticals”). It is also worth noting that the ICH is also trying to work closely with ISO in order to transform ICH guidelines in ISO standards, applicable under the TBT agreement. See ICH Steering Committee, Proceedings, 5-10 May, 2007, Brussels, Belgium.

¹²² *Decision of the TBT Committee on Principles for the Development of International Standards*, at 6.

¹²³ See Dimitrios Katsikas, *International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceutical Products*, in Thomas N. Hale & David Held (eds.), *THE HANDBOOK OF TRANSNATIONAL GOVERNANCE: INSTITUTIONS AND INNOVATIONS* (Cambridge: Polity Press, 2011) at 93.

making to those disadvantaged”.¹²⁴ In the absence of a balanced representation of different interests, the pharmaceutical standards are likely to reflect the interests of pharmaceutical industries. The ICDRA has drawn attention to this problem and called on standard-setting bodies to find solutions.¹²⁵

Some initiatives of the ICH illustrate the desire of the latter to remedy the above legitimacy deficit. The most significant attempt in this regard is the wide-range consultation conducted in the process of elaboration of ICH standards. Draft guidelines are sent to non participating countries through the WHO’s contact list and comments are invited on the ICH website. As the developing countries are effectively represented in the WHO, such initiatives may permit them to voice their concerns. However, these initiatives fall short of meeting legitimacy concerns. To start with, there is no guarantee that views or comments submitted to ICH are in fact considered. The latter only undertakes to transmit “all comments received to the appropriate [Expert Working Groups] for consideration”. As pointed out by Prof. Stewart,

“A central purpose of procedural regard - for example, procedures allowing those affected to submit evidence, analysis and views to decision makers, and requiring decision makers to respond to these submissions in the process of giving explanations and reasons for their decisions - is to help ensure that the affected are fairly or appropriately treated in the decision made, in accordance with applicable decisional norms.”¹²⁶

When no explanation or reason is given with regard to comments submitted, it is difficult to determine to what extent those comments are actually taken into account.¹²⁷

Another reason for concern is related to the level of technical complexity that pharmaceutical standards display. As observed by a commentator, effective participation of the affected actors requires the information be “accessible [and] intelligible”.¹²⁸ Not all actors, especially if they are based in developing countries, possess the level of expertise that a meaningful participation would require.

The ICH has launched several initiatives to remedy such shortcomings. As mentioned above, to ensure a better representation of the interests of the non-ICH countries, a Global Cooperation Group (GCP) was set up as a subcommittee of the ICH Steering Committee in 1999. The purpose of the GCP is to “act as the primary representative of ICH Steering Committee outside the ICH regions, and equally as such as a conduit for non-ICH parties to the ICH Steering Committee”.¹²⁹ The lack of the necessary level of expertise in non-ICH regions remains, however, a significant hurdle to a meaningful participation of

¹²⁴ Richard Stewart, *Accountability, Participation, and the Problem of Disregard in Global Regulatory Governance*, Paper presented at New York University - Law School – International Legal Theory Colloquium on Interpretation and Judgment in International Law, February 7, 2008 (at 5-6).

¹²⁵ See in particular, *Recommendations of the 12th International Conference of Drug Regulatory Authorities*, Seoul, 2006, para. 5 (“Any international mechanism or organization which develops guidance relevant for countries outside their own regions should ensure that those countries are made aware of these developments and are directly approached to take part in the consultation process.”)

¹²⁶ Stewart, *supra* note 124.

¹²⁷ A 2001 WHO Report highlighted that “[t]he views, priorities, and needs of the majority of WHO Member States [had] only sporadically been taken into consideration.” (WHO, *The Impact of Implementation of ICH Guidelines in Non-ICH Countries*, Report of a WHO Meeting, Geneva, 13-15 September 2001, p. 16). Although, the ICH has taken some steps to meet this criticism since 2001, there is no reason to think that the situation described by the WHO has changed radically.

¹²⁸ Bärbel R. Dorbeck-Jung, *Challenges to the Legitimacy of International Regulation: The Case of Pharmaceuticals Standardisation*, in Andreas Follesdal, Ramses A. Wessel & Jan Wouters (eds.), *MULTILEVEL REGULATIONS AND THE EU: THE INTERPLAY BETWEEN GLOBAL, EUROPEAN AND NATIONAL NORMATIVE PROCESSES* (Leiden/Boston, Martinus Nijhoff, 2008) 51, at 56.

¹²⁹ ICH Global Cooperation Group, “Terms of Reference”, Osaka Meeting, November 2003.

those regions. Although the ICH has offered a number of training opportunities,¹³⁰ a structural problem of such magnitude is unlikely to disappear in a foreseeable future.

2) Legitimacy cannot, however, be limited to its procedural dimension. The latter refers only to what has been aptly described as “input legitimacy”.¹³¹ Although the procedural and substantive dimensions of legitimacy are clearly related,¹³² the lack of procedural legitimacy does not automatically entail the conclusion that the substantive legitimacy is also lacking. What has been called “output legitimacy” can still be ensured if the decisions actually “take into account the specific interests of diverse affected groups”.¹³³

That being said, it is difficult to see why an industry-driven entity such as the ICH would be willing to sacrifice its business interests in order to meet the interests of developing countries. There can be no doubt that this is an important concern. As a WHO Report pointed out, the fact that the ICH standards are increasingly perceived as *de facto* global standards¹³⁴ implies a significant risk for developing countries as the drug regulation authorities and generic manufacturers in those countries may become less sensitive to local priorities by devoting limited resources to “unnecessary expenses entailed by the adoption of more costly regulatory requirements”.¹³⁵

This is, however, not to say that pharmaceutical standards can enjoy no substantive legitimacy. Substantively, these standards are largely supported because they are backed up with the authority of science - since pharmaceutical standards incorporate a high level expertise, they are seen by relevant actors as “expert-driven” rather than generated as a result of “political bargaining” or governed by business considerations and accordingly enjoy social support.¹³⁶

Does it mean that pharmaceutical standards enjoy an unshakable science-based legitimacy? Such a conclusion would be unwarranted since there are at least two reasons which invite some skepticism. The first reason is related to the very way in which science operates. It is nowadays widely accepted that science cannot claim absolute objectivity because scientific findings are not merely a function of immutable natural laws, but depend to a significant extent on disciplinary paradigms shared by a given community of scientists.¹³⁷ Emerging on the basis of “[similar] technocratic training, similarities in

¹³⁰ APEC Q8-10 Quality Guideline Workshop, September 2007, Seoul, Korea ; APEC Workshops on Review of Clinical Trials, March 2008 / March 2009, Bangkok, Thailand ; APEC Workshops on Clinical Research Inspections, May 2008.

¹³¹ Iversen Werle, *Promoting Legitimacy in Technical Standardization*, 2 SCIENCE, TECHNOLOGY AND INNOVATION STUDIES (2006) 19-39.

¹³² John Rawls, *POLITICAL LIBERALISM* (Columbia University Press, 2005, at 421). See also Stewart, *supra* note 124, at 5-6 (“[I]t may not be sufficient to satisfy procedural regard for the decision-makers to permit submissions and respond to them in decisions, if the decision itself treats the affected with manifest injustice. We want to say that the decision-makers have not really considered the interests of the affected, for if they had they would have made a different decision. This does not mean, however, that procedure collapses into substance. While the governing decisional norms may place constraints on decisional outcomes and the treatment of those affected, they are typically so numerous and general as to allow decision-makers wide latitude in striking the balance among competing considerations, interests and values in given situations.”)

¹³³ Werle, *supra* note 131, at 25.

¹³⁴ See John Abraham & Tim Reed, *Globalization of Medicines Control*, in John Abraham & Helen Lawton Smith (eds.), *REGULATION OF THE PHARMACEUTICAL INDUSTRY* (New York, Palgrave Macmillan, 2003) at 85 (noting that “there is no doubt that many in the transnational pharmaceutical industry regard ICH as the first step towards global harmonization of regulatory standards”).

¹³⁵ See WHO, *supra* note 127, at 16.

¹³⁶ Arts & Kerwer, *supra* note 18 at 147.

¹³⁷ Thomas Kuhn, *THE STRUCTURE OF SCIENTIFIC REVOLUTIONS* (Chicago, University of Chicago Press, 3rd ed, 1996) at 50-51.

scientific outlook and shared disciplinary paradigms”¹³⁸, a community of scientists sees reality in a particular way because it shares “a dominant way of looking at social reality, a set of ... symbols and references, mutual expectations and a mutual predictability of intention”.¹³⁹ Pharmaceutical standard-setting is an area in which such “epistemic communities”¹⁴⁰ are particularly powerful because of the high level complexity that such an activity implies.¹⁴¹

Since it is as much a product of a particular way of training and shared beliefs as of the way things really are, science can claim no absolute objectivity.¹⁴² Public health risk assessment is not exception to this. Risk assessment inevitably involves a probabilistic analysis and as in all probabilistic analyses gaps in the data are filled by various assumptions influenced by particular epistemic cultures and normative values. They are therefore disputable, and in fact often disputed. More than science, risk assessment involves what Weinberg called a ‘trans-science’: a science that looks at questions that are laid out in a scientific language but are ‘unanswerable’ by it.¹⁴³ A proper assessment of the science’s claim to objectivity is particularly relevant in the context of pharmaceuticals, as public authorities, when governing public health issues, are to give a proper weight to some non-scientific considerations such as public opinion, culture, or historical tradition.

The second reason why the taken-for-granted nature of scientific findings supporting pharmaceutical standard-setting should be problematized is related to the intimate link between regulatory authorities and pharmaceutical industries. As reported by a commentator, regulatory cultures are often affected by industry via what is called “the revolving door” – officials working for regulatory authorities start their career in industry, and then get recruited by regulatory authorities before moving back into industry at a higher position.¹⁴⁴ The reason why such a situation is worrisome is that experts whose advice are sought to set forth pharmaceutical standards often work for both regulatory authority and pharmaceutical industry or at least have some sort of interest in pharmaceutical industry.¹⁴⁵ This gives rise to conflicts of interests and suggests caution with respect to scientific backup for pharmaceutical standards.

But the purpose of this paper has not been to defend the legitimacy of pharmaceutical standards, but to identify the kind of legitimacy those standards enjoy and assess the extent to which they differ from traditional modes of global regulations. The preliminary conclusion I would like to offer is that pharmaceutical standards present the same concerns of democratic legitimacy as many traditional modes

¹³⁸ John Ruggie, *International Responses to Technology: Concepts and Trends*, 29 INTERNATIONAL ORGANIZATION (1975) at 570.

¹³⁹ *Id.*, at 569-570.

¹⁴⁰ The term is here being used in the sense introduced by Peter M. Haas who defined it as referring to “a network of professionals with recognized expertise and competence in a particular domain and an authoritative claim to policy-relevant knowledge within that domain or issue-area” (Peter M. Haas, *Introduction: Epistemic Communities and International Policy Coordination*, 46 INTERNATIONAL ORGANIZATION (1992) at 3).

¹⁴¹ Bryan Walser, *Shared Technical Decision-making and the Disaggregation of Sovereignty: International Regulatory Policy, Expert Communities, and the Multinational Pharmaceutical Industry*, 72 TULANE LAW REVIEW (1998) at 1597.

¹⁴² Khun, *supra* note 137, at 50.

¹⁴³ Alvin M. Weinberg, *Science and Its Limits: The Regulator’s Dilemma*, 2 ISSUES IN SCIENCE AND TECHNOLOGY (1985) at 59-72.

¹⁴⁴ John Abraham, *The Pharmaceutical Industry as a Political Player*, 360 THE LANCET (2002) at 1498. See also Mary E. Wiktorowicz, *Emergent Patterns in the Regulation of Pharmaceuticals: Institutions and Interests in the United States, Canada, Britain, and France*, 28 JOURNAL OF HEALTH POLITICS, POLICY AND LAW (2003), 615.

¹⁴⁵ Abraham, *supra* note 144, at 1499-1500.

of regulation at the international level. However, they enjoy a specific type of legitimacy based upon science which needs to be problematized.

D. The World of Pharmaceutical Standards: A Fragmented World with No Coherence?

As described above, the pharmaceutical standards are produced by many bodies with no formal task-sharing, nor a formal hierarchy. The overall result is a fragmented normative process which understandably poses a risk of incoherence.

Although accurate in principle, this observation needs to be qualified in two respects. First of all, the problem of fragmentation is not at all confined to the world of pharmaceutical standards. Even traditional international law has never possessed a centralized legislative process – which accounts for the endless debates about the fragmentation of international law.¹⁴⁶ There is no hierarchy between custom and treaties, nor is there any straightforward rule for deciding the issue of conflicts between different treaties. There is also no organizing principle governing the relationship between multiple international tribunals,¹⁴⁷ as a result of which there is no principled solution for determining the choice between conflicting holdings of different tribunals.¹⁴⁸

Second, although there is no formal hierarchy between different regimes, there are reasons for thinking that the risk of mutually inconsistent standards may not be practically significant. Many factors account for this. To start with, there is a significant interaction between different regimes. For instance, the WHO is an observer at the ICH Steering Committee; the CIOMS serves as “a think tank, a reservoir of ideas for ICH”¹⁴⁹; there is also strong cooperation between PIC/S and the ICH.

Another reason is that experts who work on pharmaceutical standards form a community whose members actively interact. There is in fact an “invisible college of scientists”¹⁵⁰, who, despite their individual trajectories, link different regimes among them because their evaluative expertise circulates, all the more so considering that the same experts often act within different regimes “thanks to a variety of

¹⁴⁶ See *Fragmentation of International Law: Difficulties Arising from the Diversification and Expansion of International Law*, Report of the Study Group of the International Law Commission, A/CN.4/L.682.

¹⁴⁷ Jonathan Charney, *Is International Law Threatened by Multiple International Tribunals?*, 271 RCADI (1998)101-382; Pierre-Marie Dupuy, *L'unité de l'ordre juridique international*, 297 RCADI (2002) 9-490 ; Syméon Karagiannis, *La multiplication des juridictions internationales: un système anarchique?*, in LA JURIDICTIONNALISATION DU DROIT INTERNATIONAL (Paris, Pedone, 2003) 7-161. See also the special issue of the NEW YORK UNIVERSITY JOURNAL OF INTERNATIONAL LAW AND POLITICS, 1999, vol. 31, No 4.

¹⁴⁸ *SGS Société Générale de Surveillance S.A. v. Republic of the Philippines*, ICSID Case No. ARB/02/6, Decision of the Tribunal on Objections to Jurisdiction, 29 January 2004, 97 (“There is no hierarchy of international tribunals, and even if there were, there is no good reason for allowing the first tribunal in time to resolve issues for all later tribunals”). See also, *Prosecutor v. Tadić, Appeals Chamber*, Decision on the Defence Motion for Interlocutory Appeal on Jurisdiction, 2 October 1995, para. 11; *Prosecutor v. Zejnir Delalic et al.*, Case No.: IT-96-21-A, ICTY, Appeals Chamber, 20 February 2001, para. 24; *The Right to Information on Consular Assistance. In the Framework of the Guarantees of the due Process of Law*, I/A Court H.R., Advisory Opinion OC-16/99 of October 1, 1999. Series A No. 16, para. 61.

¹⁴⁹ See Demortain, *supra* note 65, at 102 (“Since the ICH progressively became the central standard-setting body in pharmaceutical regulation, the CIOMS has been used for sort of pre-ICH meeting expert consultations.”).

¹⁵⁰ *Id.* at 35 (“The notion of invisible college serves here to show that scientists and their evaluative knowledge circulate, and that they link together more formal standard-setting arenas. It is used to speak about a particular pattern of association and knowledge production that mixes institutional precariousness and epistemic power.”).

identities that they can use – researchers, scientific advisers, industry consultants, standard- setters and so on”.¹⁵¹ This phenomenon has the effect of potentially reducing the risk of significant inconsistency.

Also significant is the phenomenon of “cross-fertilization” between different standards. To enhance the legitimacy and authority of their standards, standard-setting bodies often rely on existing standards and build on them. For instance, many ICH guidelines refer to the work of the CIOMS and the PIC/S and the WHO largely relies on the ICDRA recommendations.¹⁵² This strategy seems to reduce the risk of inconsistent standards to a significant extent.

Finally, there is an informal task-sharing among at least some regimes. For instance, to the extent that the WHO pharmaceutical standards and guidelines primarily focus on essential drugs,¹⁵³ the standard-setting activity of the WHO is clearly oriented towards resource-limited countries. With the ICH focusing on the industrialized world and research-intense products, this exhibits an informal task-sharing between the two most important standard-setting bodies.¹⁵⁴

CONCLUSION

A tentative conclusion can be drawn from the foregoing. Although pharmaceutical standards challenge, to a certain extent, the traditional picture of international regulatory governance, it seems that the radical transformation thesis needs to be qualified. Many features of pharmaceutical standards which are described as a significant novelty can be traced back to experiences which have already been seen at the international level. As specified earlier in this paper, this is the case with the norm-like nature of pharmaceutical standards, compliance with them or the issue of coherence.

This is, however, not to say that pharmaceutical standards pose no challenge on the conceptual and practical planes. As shown above, the scientific basis of the legitimacy of these standards should not be taken for granted, since many factors, other than science, impact the making of pharmaceutical standards. Consequently, considering the uneven representation in some standard-setting bodies of different interests affected, it is important to problematize the science-based legitimacy of pharmaceutical standards. However, such tasks can only be appropriately carried out once pharmaceutical standards are properly conceptualized, which implies, among other things, properly comparing these standards with existing regulatory experiences.

¹⁵¹ *Id.* at 11. See also at 102 (“[w]ithin ICH, the same people that meet in CIOMS as independent experts meet as industry or government representatives.”).

¹⁵² There are many practical illustrations for this cross-fertilization: for example, PIC/S work on Active Pharmaceutical Ingredients was largely relied on by the ICH (See, for instance, PIC/S Blueprint, 2005, para. 8: “PIC/S was also instrumental in elaborating a first draft for the ICH Q7A Guide on APIs [...] After further work by PIC/S, the draft was transferred to ICH in order to allow industry to become involved in further refinement of the document, and its finalisation in November 2000. PIC/S adopted the ICH GMP Guide as a stand alone PIC/S GMP Guide on API.”).

¹⁵³ The WHO list of essential medicines is based on a concept developed in the 1970s and defined as all medicines “that satisfy the priority health care needs of a population and are selected with regard to disease prevalence, safety, efficacy, and comparative cost-effectiveness”. See WHO, *The Selection and Use of Essential Medicines*, Technical Report Series 914, 2003.

¹⁵⁴ The WHO Expert Committee on Specifications for Pharmaceutical Preparations underlines that “while ICH standards were important in specifying requirements for pharmaceutical manufacturers of new chemical entities, WHO had an important role in adopting and adapting ICH standards for developing countries. The Committee therefore endorsed the need for WHO to intensify its efforts to develop international standards on the approval of generic products in consultation with the generic industry, related organizations and national authorities. This would improve access to quality essential drugs.” (WHO Expert Committee on Specifications for Pharmaceutical Preparations, Technical Report, Thirty-seven Report, WHO Technical Report Series 908, 2003, at 17).