

Industry Associations and Transnational Rule-Making: The ICH

Ayelet Berman¹

Draft – for presentation at the ASIL IOIG conference on ‘Industry Associations and Transnational Governance’, Rutgers Law School, 10 June 2016

Abstract

The ICH is a network of drug regulatory authorities and pharmaceutical industry associations that harmonizes standards for the registration of drugs. This paper addresses the advantages and the risks associated with such public-private cooperation: Why do regulators cooperate with industry associations? And what are the risks associated with such cooperation? I address, on the one hand, the dependency of regulators on industry expertise, and, on the other hand, the capture of regulators by industry interests as well as some of the distributional consequences of industry-dominated standards. Finally, how can we balance between these conflicting needs and risks to achieve effective yet fair standards?

1. What is the International Conference on Harmonization (ICH)? What does it do?

Background

The ICH was set up in 1991. The ICH’s historical purpose has been to harmonize the technical guidelines for new pharmaceutical product registration.² The harmonized guidelines are adopted into the domestic regulatory systems of the members as guidelines or regulations. Nowadays, harmonization is almost complete, and the ICH’s main goal is promoting the dissemination of ICH guidelines in non-ICH countries.³ The standards are considered the gold standard and are followed globally.

Why harmonize? As a general rule, before a new drug can be sold, the national regulatory authority of the country where it will be used must authorize it. Normally, a law setting out the principal requirements for marketing authorizations sets out that the safety, efficacy and good quality of the drug at hand need to be demonstrated. These principles are very general and, as such, the technical tests that must be done to demonstrate compliance are set out in regulations or guidelines.

Historically, ICH member countries had similar statutory requirements (i.e. that a drug be safe, effective and of good quality), but discrepancies in these technical requirements (i.e. which tests and procedures must be undertaken to demonstrate that the product is indeed safe, effective and of good quality) led to duplicate testing (as for the same drug different tests needed to be conducted to receive market authorization in different countries). This led to high costs and delays in the introduction of the same drugs in

¹ Post Doctoral Research Fellow, Graduate Institute of International and Development Studies, Geneva

² ICH, *The Value and Benefits of ICH to Drug Regulatory Authorities: Advancing Harmonization for Better Health* 1 (2010), available at http://www.ich.org/fileadmin/Public_Web_Site/News_room/C_Publications/ICH_20_anniversary_Value_Benefits_of_ICH_for_Regulators.pdf (last visited Feb. 28, 2014).

³ Interview with Swissmedic regulator, 14 June 2010 (Bern).

different countries. Politically, these “drug delays” became a major issue in the U.S. with the outbreak of the AIDS epidemic in the 1980’s. This led the FDA, which historically had never agreed to cooperate with foreign regulators, to change its attitude.⁴ These TRNs were, hence, set up to harmonize such diverging requirements and to develop harmonized standards. As such, when a test is generated in one part of the world, it can also be accepted in another part, and it speeds up the approval (and the marketing) process, benefiting industry as well as regulators and patients.

Members

Originally, the members were drug regulatory authorities and research and development (R&D) based industry associations from the U.S., EU, and Japan. Regulators and industry associations enjoy an equal partnership. The regulatory authorities are the U.S. Food and Drug Administration (FDA),⁵ the European Commission DG Health and Consumers, the European Medicines Agency (EMA),⁶ the Japanese Ministry of Health, Labour & Welfare (JMHLW) and the Japanese Pharmaceuticals and Medical Devices Agency (JPMDA).

The R&D industry associations represent R&D drug companies (that is, companies that develop new, innovative (patent protected) drugs). The R&D industry members are the Pharmaceutical Research & Manufacturers Association of America (PhRMA), the European Federation of Pharmaceutical Industries' Associations (EFPIA) and the Japanese Pharmaceutical Manufacturers Association (JPMA).⁷

ICH governance has recently been reformed – I address that below.

2. Why are regulators collaborating with industry associations?

Why are regulators, seeking to harmonize their national standards, collaborating with industry associations? The main driver is the regulators’ need and desire to develop effective standards. To this end, the expertise of the industry is needed.

Expertise

With the increasing complexity of products and their rapid change, as well as limited governmental financial resources, which make it ever more difficult for regulators to

⁴ Ayelet Berman "The Public-Private Nature of Harmonization Networks", presented at the Informal International Lawmaking (IN-LAW) Workshop, 17-18 March 2011, Netherlands Institute for Advanced Study in the Humanities and Social Sciences (NIAS), Wassenaar, the Netherlands, available as a CTEI working paper at http://graduateinstitute.ch/webdav/site/ctei/shared/CTEI/working_papers/CTEI-2011-06.pdf (last visited Mar. 2, 2014).

⁵ Technical experts are drawn from FDA’s Centre for Drug Evaluation and Research (CDER) and the Centre for Biologics Evaluation and Research (CBER).

⁶ Initially it was the EC Committee on Proprietary Medicinal Products.

⁷ ICH, *Steering Committee*, available at <http://www.ich.org/about/organisation-of-ich/steering.html> (last visited Feb. 28, 2014).

keep up and be up to date on technical matters,⁸ regulators are increasingly dependent on business for technical expertise and information. To overcome this information asymmetry, governments collaborate with business actors.⁹ Consequently, public-private collaboration have become common in many areas of global governance, such as in the financial sector, telecommunications, energy markets and the automobile industry¹⁰ (think say of ICANN, WADA, IUCN, WIPO, ISO).¹¹

The same logic explains the inclusion of industry associations in the ICH. Drug regulators do not have the necessary information to make informed judgments and independent assessments about medical products and are dependent on industry for information.¹² The industry undertakes 95% of drug development, and it is therefore ahead of regulators in expertise and when it comes to new scientific developments.¹³ Regulators rely on industry for information on topics such as toxicology, clinical trials, epidemiology, etc.¹⁴ ¹⁵ The FDA stressed these factors, saying, "... the speed of product development also is accelerating ... But ... the Agency [has] very little time to develop a regulatory framework to handle new technologies. Thus, it is imperative for FDA to continue to engage in close interaction with industry ..."¹⁶ And that "[p]roduct complexity continues to increase. FDA-regulated products will be characterized by unprecedented technological sophistication ... FDA must have access to the necessary scientific expertise to be able to address the complexity of these new products, and to provide sound regulatory decisions..."¹⁷

⁸ Tim Bueth, *Private Regulation in the Global Economy: A (P)Review*, 12 BUSINESS AND POLITICS, 4 (2010); Tim Bueth and Walter Mattli, International Standards and Standard Setting Bodies, in THE OXFORD HANDBOOK OF BUSINESS AND GOVERNMENT 448, 453 (David Coen *et al.* eds., Oxford University Press, 2009).

⁹ Fabian Amtenbrink, *Towards an Index of Accountability for Informal International Lawmakers?*, in INFORMAL INTERNATIONAL LAWMAKING, (Joost Pauwelyn, et al. eds., Oxford University Press, 2012) at 339.

¹⁰ Tim Bueth & Walter Mattli (2009), in THE OXFORD HANDBOOK ON BUSINESS AND GOVERNMENT, *supra*. Walter Mattli, *Public and Private Governance in Setting International Standards*, in GOVERNANCE IN A GLOBAL ECONOMY: POLITICAL AUTHORITY IN TRANSITION 209, 225 (M. Kahler & D.A. Lake eds., Princeton University Press, 2003).

¹¹ GLOBAL ADMINISTRATIVE LAW: THE CASEBOOK (2012), (Sabino Cassese, et al. eds., IRPA, IILJ, 2012) at XXV.

¹² Eloy Anello (WHO), *A Framework for Good Governance in the Public Pharmaceutical Sector* (October 2008), available at <http://www.who.int/medicines/areas/policy/goodgovernance/WHO-GGMframework.pdf> (last visited Mar. 3, 2014).

¹³ This point was raised in many interviews. In most countries, except for the FDA, regulators first hear about a new drug when a request for approval is submitted. Therefore, the industry is ahead of regulators in all scientific matters. See also European Medicines Agency, *Overview of Comments Received on Draft Guideline "Procedure for EU Guidelines and Related Documents within the Pharmaceutical Legislative Framework"*, Doc. Ref. EMEA/125817/2004 (24 June 2005), available at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/10/WC500004015.pdf (last visited Mar. 3, 2014).

¹⁴ John Abraham, *The Pharmaceutical Industry as a Political Player*, *The Lancet* 1498 (2002).at 1498.

¹⁵ Joe Collier & Ike Iheanacho, *The Pharmaceutical Industry as an Informant*, 360 THE LANCET 1405 (November 2, 2002).

¹⁶ F.D.A., FDA Plan for Statutory Compliance 63 FR 65000 (24 November 1998).

¹⁷ *Id.*, at 65005 and 65006 (italics added).

Consequently, the inclusion of industry associations is driven by the need or desire to develop effective, scientifically updated standards. That said, the inclusion of industry associations alongside regulators raises several problems, which we look at next.

3. What problems arise when regulators collaborate with industry associations?

While the involvement of industry associations is helpful in achieving effective standards, their inclusion raises several problems from a public interest perspective. The problems I want to concentrate on are (1) the risk of capture, and (2) the distributional consequences.

A. Risk of Capture

The pharmaceutical sector is prone to regulatory capture because regulators – as mentioned above – do not have the necessary information to make informed judgments and independent assessments about medical products and are dependent on industry for information.¹⁸ But while we would like to think of scientific information as neutral, that is not always the case, and so the interests of the parties may come into play.

The non-alignment of industry interests and the public interest. Regulators are expected to protect the public interest, but industry associations promote their commercial interests. The efforts of the industry have led to the development of many medical products that are of great benefit to humans. Thus, at least to some extent the commercial interests of the industry and the public health interests of patients correspond.¹⁹ However, in reality, patients' and industry's interests often do not coincide. The goal of medical companies is to make profit, and so while medical companies want the safety and efficacy standards of regulators to be high enough to avoid frequent medical disasters, which brings the industry into disrepute, they do not want it so high that it would threaten their commercial viability. Thus, the interests of the industry can sometimes diverge, or even conflict, with public health.²⁰

In the case of the ICH, the industry's dominance – coupled with the lack of representation of patients and consumer interests – raises the concern that the public interest in safe medical products is undermined due to the industry's interest in cost reduction.²¹ It suggests that the ICH may have difficulty maintaining a public health-

¹⁸ Eloy Anello (WHO), *A Framework for Good Governance in the Public Pharmaceutical Sector* (October 2008), available at <http://www.who.int/medicines/areas/policy/goodgovernance/WHO-GGMframework.pdf> (last visited Mar. 3, 2014).

¹⁹ John Abraham, *The Pharmaceutical Industry as a Political Player*, *THE LANCET* 1498, 1498 (2002).

²⁰ *Id.*, at 1498. See also, *Transparency: BMJ Report finds Industry Reviews of Medicines Less Transparent than Non-Profit Reviews*, *REGULATORY AFFAIRS JOURNAL-PHARMA* (10 October 2006) (on file with the author).

²¹ On public interest theory of regulation, see R. BALDWIN *et al.*, *UNDERSTANDING REGULATION: THEORY, STRATEGY, AND PRACTICE* (Oxford University Press, 2nd ed., 2011); For a similar view, see Abraham (2002), *supra*, at 1498. On capture theory, see M. BERNSTEIN, *REGULATING BUSINESS BY INDEPENDENT COMMISSIONS* (Greenwood Press, 1977). See also Eyal Benvenisti, *Towards a Typology of Informal International Lawmaking Mechanisms and their Distinct Accountability Gaps*, in *Informal International Lawmaking* (Joost Pauwelyn, et al. eds., Oxford University Press, 2012) at 306 (saying that “the diminishing domestic accountability of IN-Lawmaking by governments raises the concern about interest group capture, and hence the adoption of inefficient, inequitable policies”).

oriented approach, and that it is prone to “regulatory capture” by industry interests.²² To be sure, the ICH has already been criticized for being an “industry–driven process”,²³ and for not taking the interests of patients, academia, health professionals, etc. appropriately into account.²⁴

B. Distributional Effects

Due to globalization, we are in a time of interconnectedness and interdependence. Therefore, ‘club’ standards may have effects – distributional effects – on states and communities that are not members of the club. That has also been the case of the ICH. While the ICH is a club of regulators and industry associations from developed countries, in practice, ICH standards have distributional effects, with consequences for countries and communities that are outsiders. We next take a look at two examples:

1 Distributional Effects on Competing Industries: The Generic Drugs Industry

ICH guidelines are set by R&D industry associations, but affect the generic industry too, and grant the R&D industry a competitive advantage over the generics industry:

R&D and generics industries compete: The interests of the different segments in the medical product industry are not aligned, and are often fragmented with competing interests. This is most pronounced in the pharmaceutical industry. There, the R&D industry develops new drugs (which are then patented) and competes with the generics industry, which manufactures drugs whose patent protection has expired. As such, the R&D industry will always seek to prevent or delay the entry of generic medicines.

R&D industry is setting the rules for the generic industry too: ICH regulators write the standards together with the R&D industry, and with their interests in mind. Nevertheless, ICH standards are considered the ‘gold standard’, the result being that drug regulatory authorities – rather than developing special standards for generic medicines – have subjected the generics industry to ICH guidelines in the market approval process.²⁵ It is now customary for regulators to apply ICH quality guidelines for the approval of generic drugs.²⁶ Thus, in order to get approved, applicant generic drugs must comply with most ICH standards. And so while the historical purpose of ICH guidelines had been to set harmonized standards for the approval of new, innovative, patent protected drugs, in practice, they affect the generic drug market too.

²² WHO, *Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries*, WHO/EDM/QSM/2002.3 (13-15 September 2001), available at <http://apps.who.int/medicinedocs/pdf/h2993e/h2993e.pdf>.J. (last visited Mar. 3, 2014); Abraham & T. Reed, *Trading Risks for Markets: the International Harmonisation of Pharmaceuticals Regulation*, 3 HEALTH, RISK & SOCIETY 113 (2001).

²³ Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries, *supra*, at 16.

²⁴ Lori M. Wallach, *Accountable Governance in the Era of Globalization: The WTO, NAFTA, and the International Harmonization of Standards*, 50 University of Kansas Law Review 823 (2001-2002).; Report of a WHO Meeting: *The Impact of Implementation of ICH Guidelines in Non-ICH Countries*, *supra*, at 16.

²⁵ Two examples : (1) ICH Q3A (“Impurities in New Drug Substances”) and Q3C (“Impurities : guidelines for the residual solvents”) were developed for new products but their application has been extended by European authorities to cover all products, including generics, registered in the EU; (2) ICH Q7A on GMP for APIs expands requirements for manufacturers of pharmaceutical active starting materials, and so creates increased rigidity in the starting material supply system, with consequent effects on starting material prices and availability.

²⁶ Interview with WHO observer on ICH Steering Committee, Geneva, 2011.

ICH standards affect the generics industry: The generic drug industry, has, hence been significantly affected by ICH standards. This holds true not only for the generic industry in ICH member countries, but also for generic drug manufacturers in non-member developing countries (which follow ICH standards too)– where most of the drug supply is of a generic nature.²⁷ Moreover, this effect has become more important in the past two decades with the significant growth of the generic drug market.²⁸ Due to this growth in market share, ICH standards have, therefore, had an even more significant effect on the generics industry.

The ICH guidelines make it harder for the generic industry to compete against the R&D industry: The R&D industry is a larger, wealthier industry and has more resources than the generic industry. Standards may be too costly or resource intensive for the generic industry to comply with, such as due to a lack of appropriate facilities. Thus, some of the requirements are practically unreachable for the generic industry.²⁹ At the same time, scientific experts have stressed that due to the ‘copying’ nature of the generic drugs, they require less testing than new, innovative drugs.³⁰ Hence, generic drugs are required to comply with ICH standards that are often unnecessarily demanding and costly for them. This, in turn, affects their market share. Moreover, it also affects access to medicines, mostly in developing countries that are dependent on generic medicines for their essential medical needs.³¹

To conclude, the ICH standards are not neutral in their distributional effects, and they give the R&D industry a competitive advantage over the generics industry. Is this fair?

2 *Distributional Effects on Non-Commercial Drug Development: Drugs for Neglected Diseases in Developing Countries*

One of the central health problems in developing countries is that for many diseases, medicines are non-existent. These diseases, commonly referred to as “neglected diseases”, have generally been defined as communicable, tropical diseases such as malaria, sleeping sickness, chaga sieases and leishmaniasis, for which there is essentially no pharmaceutical research and development.³² Indeed, only a small fraction of the total worldwide expenditure on health research and development is devoted to the development of medicines for such diseases. Neglected diseases are endemic primarily in

²⁷ WHO, Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries, WHO/EDM/QSM/2002.3 (13-15 September 2001) <http://apps.who.int/medicinedocs/pdf/h2993e/h2993e.pdf>. Oxfam, Eye on the Ball: Medicine Regulation -- Not IP enforcement -- Can Best Deliver Quality Medicines, 143 OXFAM BRIEFING PAPER (2011), available at <http://www.oxfam.org/sites/www.oxfam.org/files/eye-on-the-ball-medicine-regulation-020211-summ-en.pdf> (last visited Mar. 3, 2014), at fn 57. Prescrire, ICH: An Exclusive Club of Drug Regulatory Agencies and Drug Companies Imposing its Rules on the Rest of the World, 19 PRESCRIRE INTERNATIONAL 183 (2010) and WHO, Global Harmonization and the ICH, 30 ESSENTIAL DRUGS MONITOR 1 (2001).

²⁸ Interview, IGPA official, August 2015.

²⁹ Interview IGPA official.

³⁰ Interviews with officials from Swissmedic (Swiss drug regulatory authority), WHO Essential Medicines Division.

³¹ Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries, *supra*

³² Suzanne Hill & Kent Johnson, *Emerging Challenges and Opportunities in Drug Registration and Regulation in Developing Countries* DFID Health Systems Resource Centre: Issues paper - Access to Medicines, available at <http://www.hlsp.org/LinkClick.aspx?fileticket=0TXMdaAk5KA%3D&tabid=1643> (last visited Mar. 2, 2014).

Africa, Asia and tropical regions of the Americas.³³ An estimated 1.4 billion people,³⁴ including 400 million children, suffer from one or more neglected diseases. Many of these diseases exact a large and lethal toll, with tuberculosis and malaria alone killing an estimated 2.6 million people annually. Other neglected diseases are less deadly but disable or deform.

These diseases are “neglected” as despite an ever-increasing need for medicines for the treatment of these diseases, drug development is virtually non-existent. With the emergence of a free market-based world order, commercial prospects rather than global health needs guide the direction of new drug development.³⁵ The pharmaceutical industry argues that research and development is too costly and risky to invest in low-return neglected diseases, and prefer focusing on “blockbuster” drugs for the developed world. The adverse public health consequences of this evolution for the developing (mostly tropical) world have been grave.³⁶ Given the high disease burden, developing countries urgently need research to help relieve them from such diseases.³⁷

In the past decade this has become a hot topic and there have been initiatives underway that seek to overcome this market failure through incentive packages and public-private partnerships. The buzzword is “product development partnerships”, whereby drug companies work with non-profit organizations (such as the Drugs for Neglected Diseases Initiative, the Medicines for Malaria Venture, the Meningitis Vaccine Project) and academia in drug discovery projects. Philanthropic and public funds absorb the costs and risks of drug development, and industry picks up the projects and markets and distributes them.³⁸ Thanks to such initiatives, in the past decade there has been tremendous progress in the development of drugs and vaccines for neglected diseases, and there are now dozens of candidate products in the pipeline.

Certain global initiatives to systematically deal with this problem are underway too. For example, most recently a WHO Consultative Expert Working Group issued a report on “Research and Development to Meet the Needs in Developing Countries: Strengthening Global Financing and Cooperation”. The report proposes innovative financing and cooperation options to tackle this problem, including a recommendation to reach a binding International Convention on Global R&D.³⁹

³³ Thomas Bollyky, et al., *Bridging the Gap : Improving Clinical Development and the Regulatory Pathways for Health Products for Neglected Diseases* 7Clinical Trials 719 (2010).at 722-723.

³⁴ Janice Hopkins-Tanne, *How the Search for New Drugs for Neglected Diseases is Paying Off*, 344 BMJ 18, 18 (2012).

³⁵ *Id.*, at 18.

³⁶ Patrice Trouiller et al., *Drugs for Neglected Diseases: a Failure of the Market and a Public Health Failure?* 6 TROPICAL MEDICINE AND INTERNATIONAL HEALTH 945, 945 (2001).

³⁷ Kenneth Calman, *Conducting Research Ethically in Developing Countries*, 7 DRUG DISCOVERY TODAY 1155 (December 2002).

³⁸ Janice Hopkins-Tanne, *How the Search for New Drugs for Neglected Diseases is Paying Off*, 344 BMJ 18 (2012).at 18.

³⁹ WHO, *Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination. Report of the Consultative Expert Working Group on Research*

But how is all this related to the ICH? The ICH Good Clinical Practice (GCP) is the gold standard for clinical trials and it has led clinical trials to become increasingly time consuming and expensive,⁴⁰ leading in turn to a reduction in *non-commercial* clinical trials, including for neglected diseases.

The ICH GCP is an *ethical* and *scientific* quality standard for designing, conducting, monitoring, recording, analyzing and reporting clinical trials, that is, trials that involve the participation of human subjects.⁴¹ The ICH GCP has contributed to a reduction in clinical trials as it has increased the bureaucracy and, consequently, the costs of clinical trials.⁴² The ICH GCP introduces a rigid bureaucracy, with onerous procedural requirements for data management, documentation and reporting of trials. In comparison with the 1990s, it requires 5 to 20 times the funds to initiate a similar trial.⁴³ The ICH GCP has also led to an increase in clinical trial duration.⁴⁴ In comparison with the 1990's, it takes 4 to 5 times longer to conduct a similar trial.⁴⁵

The ICH GCP was written for *commercially* driven clinical trials (that is, clinical trials performed by the pharmaceutical industry for new medicinal products), but is now being applied in *non-commercial* clinical trials in low-income countries, including in cost sensitive clinical trials in neglected disease endemic countries.⁴⁶ The ICH GCP is excessive and overwhelming in terms of administration, oversight and documentation in such poor settings. The standard is unaffordable and unreachable in developing countries, particularly in clinical trials for neglected disease, which are highly cost sensitive endeavors. The human and financial resource capacity available to ensure a high standard of design, management, and operation of clinical trials in developing countries lags far behind that available in wealthier nations.⁴⁷ In fact, the clinical research and regulatory capacity in many neglected disease–endemic countries is rudimentary.⁴⁸ Moreover, many trials for neglected diseases, such as in Africa, even if

and Development: Financing and Coordination, (April 2012), available at http://www.who.int/phi/CEWG_Report_5_April_2012.pdf (last visited Mar. 2, 2014).

⁴⁰ Bollyky *et al.* (2010), *supra*.

⁴¹ *ICH GCP Good Clinical Practice* available at <http://ichgcp.net/> (last visited Mar. 2, 2014).

⁴² Lelia Duley *et al.*, *Specific Barriers to the Conduct of Randomized Trials*, 5 *see id.* 40 (2008).

⁴³ Salim Yusuf, *Damage to Important Clinical Trials by Over-Regulation*, 7 *CLINICAL TRIALS* 622, 624 (2010); E. Eisenstein *et al.*, *Sensible Approaches for Reducing Clinical Trials* 5 *CLINICAL TRIALS* 75 (2008).

⁴⁴ Lelia Duley *et al.*, *Specific Barriers to the Conduct of Randomized Trials* *see id.* 40.

⁴⁵ Salim Yusuf, *Damage to Important Clinical Trials by Over-Regulation*, *see id.* 622, 624 (2010).

⁴⁶ Mary Moran *et al.*, *The New Landscape of Neglected Disease Drug Development* (London School of Economics/Wellcome Trust, September 2005), available at http://www.policycures.org/downloads/The_new_landscape_of_neglected_disease_drug_development.pdf. (last visited Mar. 2, 2014), at 25-26; Bollyky *et al.* (2010), *supra* at 722.

⁴⁷ Trudie A. Lang, *et al.*, *Clinical Research in Resource-Limited Settings: Enhancing Research Capacity and Working Together to Make Trials Less Complicated*, 4 *PLoS Neglected Tropical Diseases* 619 (2010).

⁴⁸ Centre for Global Development's Working Group on Clinical Trials and Regulatory Pathways, *Safer, Faster, Cheaper: Improving Clinical Trials and Regulatory Pathways to Fight Neglected Diseases* (2011), available at

sponsored by developed countries, are *non-commercial trials* that are publicly sponsored and are, hence, severely limited in resources.⁴⁹ For non-commercial bodies the costs associated with the ICH GCP are, therefore, unaffordable.⁵⁰

A considerable amount of studies have demonstrated that the ICH GCP has been an impediment to clinical research in developing countries, with adverse effects on the development of drugs for local needs.⁵¹ In 2011, a Report issued by the Centre for Global Development's Working Group on Clinical Trials and Regulatory Pathways on "Improving Clinical Trials and Regulatory Pathways to Fight Neglected Diseases" asserted that the GCP significantly increases the delays and cost of clinical trials for candidate drugs and vaccines in the neglected disease pipeline.⁵² Many of the critics are demanding that in place of the ICH GCP, sensible GCP guidelines be developed, arguing that if sensible guidelines for clinical trials will not be developed to reverse the harm caused by the ICH GCP, the battle against disease will be severely slowed down and much of the scarce funds for clinical trials will be wasted.⁵³

While no one is contending that there isn't a need for good clinical practice, the criticism is that many of the bureaucratic requirements (e.g. mountains of papers, emails, conference calls, and other procedural aspects) add little to the quality of the process in the developing country context.⁵⁴ Moreover, the procedures are based more on technological advances than on nationally determined health priorities.⁵⁵ Finally, the ICH GCP does not address country specific issues,⁵⁶ and the fact that the ICH GCP does not take the special circumstances of developing countries into account inhibits research in those countries.⁵⁷ In sum, the ICH GCP in developing country settings has been a detriment to the development of drugs for neglected diseases.⁵⁸

http://www.cgdev.org/files/1425588_file_Bollyky_Clinical_Trials_FINAL.pdf (last visited Mar. 2, 2014), at 29.

⁴⁹Lang *et al.* (2010), *supra*, at 619.

⁵⁰Salim Yusuf, *Damage to Important Clinical Trials by Over-Regulation*, 7 *Clinical Trials* 622 (2010), at 622.

⁵¹Lang *et al.* (2011) *supra*, at 1554; Bollyky *et al.* (2010) *supra*, at 726. Nicholas J. White, *Editorial: Clinical Trials in Tropical Diseases: a Politically Incorrect View*, 11 *TROPICAL MEDICINE AND INTERNATIONAL HEALTH* 1483 (2006); Patrice Trouiller, *et al.*, *Drugs for Neglected Diseases: a Failure of the Market and a Public Health Failure?*, 6 *Tropical Medicine and International Health* 945 (2001), at 2192. Yusuf (2010), *supra* at 624.

⁵²Center for Global Development's Working Group on Clinical Trials and Regulatory Pathways, *Safer, Faster, Cheaper: Improving Clinical Trials and Regulatory Pathways to Fight Neglected Diseases*. (2011) http://www.cgdev.org/files/1425588_file_Bollyky_Clinical_Trials_FINAL.pdf at 9.

⁵³Yusuf (2010), *supra*, at 624; Lang *et al.* (2011), *supra*, at 1554.

⁵⁴Lang *et al.* (2011), *supra*, at 1554. Nicholas J. White, *Editorial: Clinical Trials in Tropical Diseases: a Politically Incorrect View*, 11 *Tropical Medicine and International Health* 1483 (2006), at 1483-1484.

⁵⁵Trouiller *et al.* (2001), *supra*, at 2192.

⁵⁶Report of a WHO Meeting: The Impact of Implementation of ICH Guidelines in Non-ICH Countries, *supra*, at para. 6.1.

⁵⁷Our understanding of the disregard by ICH GCP to the needs of developing countries is enhanced when we take a look at CIOMS guidelines. They devote more attention to the question of clinical trials in developing countries with little resources. There, local authorities must ensure that the research is responsive to the health needs and priorities of its population. It also obliges external sponsors and

4. Has the ICH responded to these problems? If so, how?

In January 2016 the ICH introduced a governance reform that fundamentally changes the ICH governance structure. The purpose of the reform, according to the ICH is to make “the ICH more transparent and accountable...and turning it into a genuinely global forum.”⁵⁹ The changes are in the legal structure (The ICH will be established as a not for profit international association under Swiss law),⁶⁰ the governance structure, in the members and observers, and in the decision-making rules. Without going into the details of the reform, I will focus on some relevant aspects of the reforms.

The new ICH association comprises several bodies. The two main ones are an assembly and a management committee. The inaugural meeting of the new assembly and management committee took place on 23 October 2015.

A. Addressing Regulatory Capture

1 Weakening the Role of Industry Associations

Whereas traditionally regulators and industry associations had an equally powerful status, the role of industry has now been formally weakened, though in practice industry will retain an important role. The ICH says that it recognizes that the participation of industry providing technical expertise was one of the key success factors of the current ICH, and that should be maintained in the new structure.⁶¹ However, in view of introducing more accountability, the role of industry is being weakened:

- ICH will become less reliant on the pharma industry funding than it is at present.⁶² One aim of the reform is for ICH to move away from traditional reliance on industry funding towards a more balanced funding mechanism. The new association will be funded through membership fees.
- Whereas previously they had identical decisional rights as the regulators, their decisional role is being weakened. Industry will no longer be entitled to vote on matters related to the adoption of ICH guidelines, and that will be the regulators’ prerogative. However, industry remains involved in guideline development in the working groups.⁶³

2 Strengthening the Generic Industry?

As a result of the effects described above, the International Generic Pharmaceutical Alliance (IGPA) has requested a seat on the ICH Steering committee.⁶⁴ With its growing market and the consequent growing impact of ICH on its production, it has become more assertive in this demand since 2013. The IGPA says that “we felt it very important

investigators to contribute to capacity building in poor host countries. (Guidelines 3 and 20, respectively).

⁵⁸ Lembit Raego, *Panel 2: ICH and Global Cooperation in the New Millennium, WHO Perspective* (Proceedings of the 5th ICH Conference, San Diego 2000), at 301 (on file with the author).

⁵⁹ Maureen Kenny, *ICH Door Closes on New Industry Members Ahead of Reforms*, SCRIP Regulatory Affairs 5 May 2015. (2015)

⁶⁰ Sean Milmo, *ICH Prepares for Major Reform* Pharmaceutical Technology at <http://www.pharmtech.com/ich-prepares-major-reform>.

⁶¹ Maureen Kenny, *Finishing Line in Sight for ICH Reforms* SCRIP Regulatory Affairs 5 May 2015. (2015).

⁶² Id.

⁶³ Id.

⁶⁴ *Global Generics Industry Continues to Fight for Equal Footing with R&D Sector at ICH*, Scrip Regulatory Affairs (2 September 2014)

that we be at the decision-making body of ICH. We shouldn't have other entities making decisions that affect our industry and we're not at the table."⁶⁵

The ICH recognizes that the generics industry is affected by ICH guidelines and the ICH recognizes that the IGPA should have a place at the table and be able to contribute. It has, therefore said that it recognizes the "possibility of wider inclusion of global industry sectors affected by ICH harmonization."⁶⁶ It has, accordingly, amended the eligibility criteria for industry members so as to open the possibility for the generic industry to join the association.⁶⁷

While that signals potential for change, IGPA is currently being refused membership in the management committee (PhRMA, EFPIA and JPMA are members).⁶⁸ Thus, the final word is still being set by the founding members.⁶⁹ The reform, hence, as of now, is disappointing for the generics industry, which had been hoping to achieve equal footing in ICH with the R&D pharma industry.⁷⁰ The IGPA has not made a decision yet whether to withdraw completely or remain playing some part even in the absence of equal footing.⁷¹ The parties are meeting mid-June 2016 and I am waiting for updates.

3 *Developing countries and marginalized interests*

While the ICH is also undergoing a reform to include new members from emerging and developing countries, the main drive is the desire to disseminate ICH standards to those countries, and issues such as effects on neglected diseases are not being discussed.

5. Question to pose:

1. The inclusion of industry associations in transnational standard setting is driven by and large by the dependency on their expertise. Their inclusion, however, introduces risks of engagement, and risks undermining the public interest (or the interests of other sectors). How do we balance between the need for effectiveness and the protection of the public interest? How can we ensure that their inclusion does not lead to bias and undermines the public interest, or the interests of weaker groups? Should we introduce rules to this end (As exist in domestic regulatory systems?) And even if we were to introduce such rules, how effective would they be in the absence of legal oversight?
2. Do clubs have any responsibility for the distributional effects that they create? What role, if at all, should they take on? Should they include affected communities and give them voice? Should they assist such communities in setting up alternative bodies for the development of standards adapted to their needs? Or are they free of any responsibility?

⁶⁵ David R Gaugh, Senior Vice President of US Generic Pharmaceutical Association, cited In Maureen Kenny, *Generics Industry Keeps up Pressure on ICH Scrip Regulatory Affairs* 5 May 2015

⁶⁶ The IGPA says that "we felt it very important that we be at the decision-making body of ICH. We shouldn't have other entities making decisions that affect our industry and we're not at the table."⁶⁶

⁶⁷ Article 12 of the New Articles of Association sets out eligibility criteria for the inclusion of international industry associations that represent members that are regulated or affected by ICH guidelines and that have been affiliated with the ICH as an observer or interested party, and appointed experts to working groups.

⁶⁸ Finishing Line in Sight for ICH Reforms *supra*P.4

⁶⁹ Id. Citing Mr, Gaugh

⁷⁰ [David R Gaugh, Senior Vice President of US Generic Pharmaceutical Association].

⁷¹ Id. Citing Mr, Gaugh