International Coordination of Human Gene Editing Regulation

Governance of Emerging Technologies Conference
May 26, 2016

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International Harmonization?

- At December 2015 global summit on human gene editing, first 4 speakers all emphasized importance of international harmonization of human gene editing regulation
  - Nobel Prize winner Dr. David Baltimore
  - President, US National Academies of Science
  - President, Royal Society of UK
  - President, Chinese Academy of Sciences

REGULATORY SCIENCE

The need for global regulatory harmonization: A public health imperative

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Margaret Hamburg is the Foreign Secretary of the U.S. National Academy of Medicine

DRUG REGULATION SERVES TO PROTECT PUBLIC HEALTH. DONE RIGHT, IT DRIVES THE ongoing assessment of product safety, efficacy, and quality and promotes the development and availability of new and better products. However, in our modern world, the mosaic of regulations that govern drug development and oversight nation by nation are creating unnecessary barriers to the efficient delivery of safe, innovative, and effective treatments to patients in need.

The need for the oversight of drugs and the creation of regulatory authorities has a long history, dating back at least to the "Apothecary Wares, Drugs, and Stuffs Act" of 1540 in England (*1*). In the years since, scientific knowledge and the scope of the pharmaceutical industry have increased, and regulatory authorities and their laws and regulations have grown in number, breadth, and complexity in almost every nation in the world. At the same time, globalization is blurring distinctions between foreign and domestic pharmaceutical products. Public health and innovation are no longer purely national issues, and the need for regulatory authorities to bring a global view to oversight grows ever more urgent. When FDA was first established many decades ago, U.S.-regulated industries were predominantly local, and the volume of imported products was low. Today, a large proportion of drugs or medical products on the shelves of a pharmacy or hospital come, at least in part, from some international source. In fact, nearly 40% of drugs and some 50% of medical devices that are used by Americans are made elsewhere. An astonishing 80% of the active pharmaceutical ingredients in drugs used in the United States are manufactured outside of its borders. Pharmaceutical companies conduct research and development (R&D) on every continent, and their supply chains are increasingly global.

Globalization has fundamentally altered the economic and innovation landscapes. This

Sci Transl Med
Volume 8(338):338ed6-338ed6
May 11, 2016

Arguments for International Governance

- International standards assure equal protection for citizens of all nations
- Uniform national requirements discourage medical tourism
- International standards provide consistent requirements for companies/scientists in the field
- Harmonized national standards prevent trade disputes (eg GMOs)
- Prevent “race to the bottom” or “risk havens”
- Regulators benefit from economies of scale and sharing resources and workload in regulatory decisions

Arguments Against International Governance

- Different social, political, and ethical norms in different countries
- Different national approaches allows for experimentation on different governance approaches
- Large resources, time and effort needed to create international standards might be better utilized in developing national oversight
- Complete agreement and compliance by all nations highly unlikely

Timing of International vs. National Standards

- Francis Fukuyama:
  - "[R]egulation cannot work in a globalized world unless it is global in scope. Nonetheless, national-level regulation must come first. Effective regulation almost never starts at an international level …." *Foreign Policy*, Mar/Apr 2002.
- But developing national regulations first may:
  - unduly delay international regime
  - be more difficult in the face of entrenched and inconsistent national regulations (e.g., GMOs)

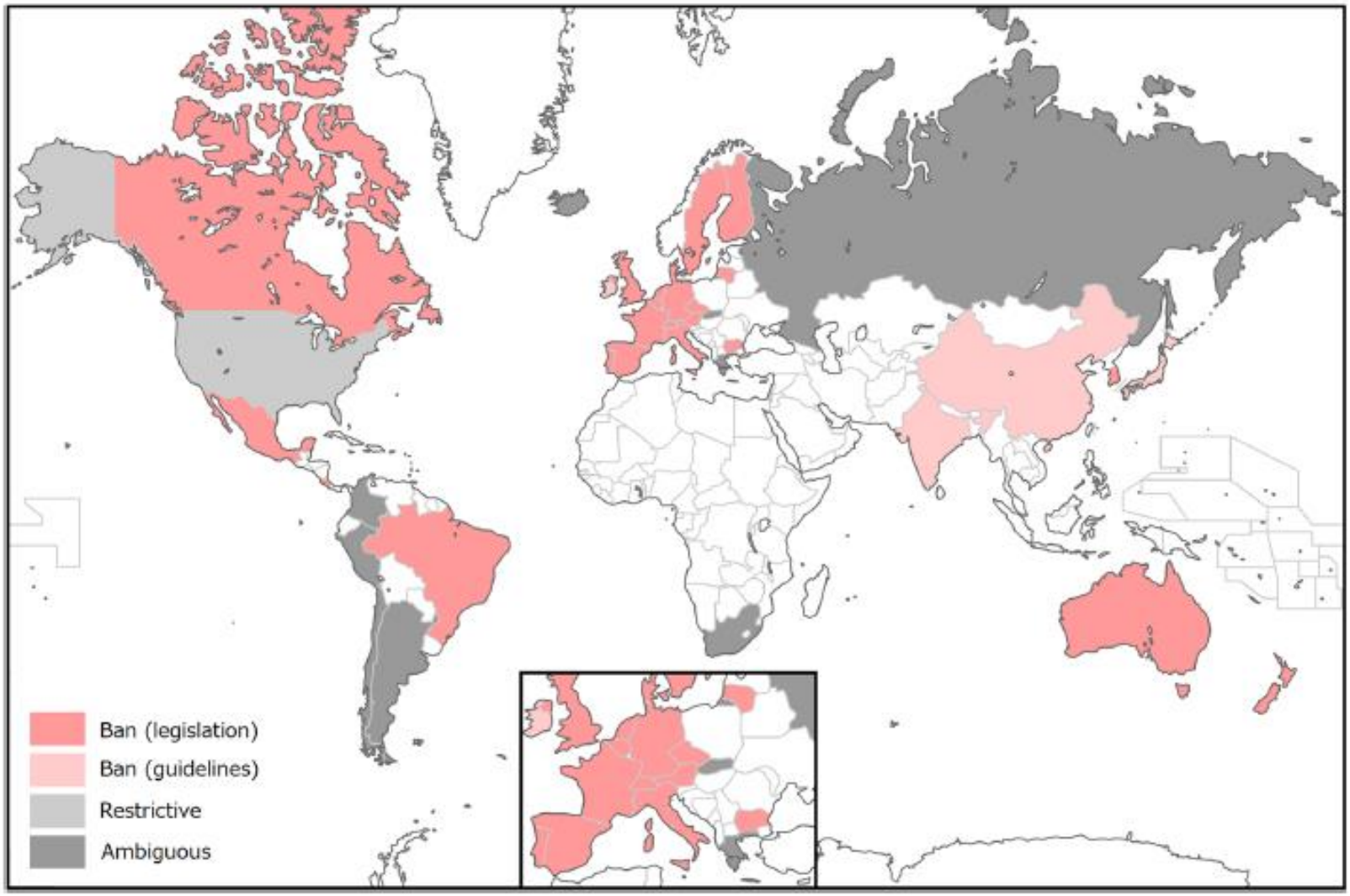

Figure 3 An international regulatory landscape regarding human germline gene modification. Thirty nine countries were surveyed and categorized as "Ban based on legislation" (25, pink), "Ban based on guidelines" (4, faint pink), "Ambiguous" (9, gray), and "Restrictive" (1, light gray). Non-colored countries were excluded in this survey. See also Additional file 1: Table S1.

Mechanisms of International Convergence

Convergence Process	Definition	Example
Transnational Regulatory Dialogue & Networking	Informal process of communication and policy learning between regulators	International Dialogue on Responsible Nanotechnology
International Coordination/ Cooperation	Non-binding international instruments such as guidelines, principles, standards	ISSCR Guidelines for Embryonic Stem Cell Research
Treaty-based Harmonization	Formal negotiation of binding treaties	UN Convention on Cloning (failed)

Adapted from Breggin et al., 2009

Traditional "Hard Law": Treaties and Other Formal Agreements

- Negotiation of international treaty requires enormous commitment of resources, time and political capital
  - e.g., climate change
- Irresoluble compliance and enforcement challenges
  - e.g., Biological Weapons Convention

Treaty Precedent: UN International Cloning Convention

- In 2001, the U.N. General Assembly established an Ad Hoc Committee to draft an international convention to prohibit human reproductive cloning
- The Human Cloning ban deadlocked in the U.N. in December 2003 due to disagreement
- U.N. Legal Committee discussed ban again in Oct. 2004; again failed to reach agreement
- Key points of disagreement:
  - Scope
  - Duration
  - Enforcement

"Transnational New Governance"

- Originates from "soft law" concept in international law
- Substantive obligations and requirements created by instruments that are not directly legally enforceable
- International scope/focus/participation
- Broadening oversight from top-down government requirements to include a much broader range of decision-makers
  - e.g., companies, researchers, NGOs, public-private partnerships, other third parties

Advantages of Transnational New Governance

- Voluntary; cooperative
- Reflexive
- Can be adopted or revised relatively quickly
- Many different approaches can be tried simultaneously
- Can be gradually "hardened" into more formal regulatory oversight

Limitations of Transactional New Governance

- Norms/standards not directly enforceable
- Risk of “whitewashing” or “greenwashing”
- Participation limitations
- Not always as flexible and adaptable as hoped
- Potential for confusion/overlap
- Less legitimacy

Examples of Transnational New Governance Tools & Examples

- Transnational regulatory dialogue and networks
  - OECD working Groups
- International regulatory harmonization committees
  - International Conference on Harmonization
- United Nations Declarations
  - UNESCO International Declaration on Human Genetic Data
- International principles
  - World Medical Association/Helsinki Principles
- International Scientific Assessment bodies
  - Intergovernmental Panel on Climate Change (IPCC)
- Professional society guidelines
  - ISSCR Guidelines for Embryonic Stem Cell Research
- International statements of policy
  - HUGO statements
- Private/industry standards
  - IGSC Harmonized Screening Protocol
- Framework conventions
  - Framework Convention on Tobacco Control

PROACTIVE INTERNATIONAL REGULATORY COOPERATION FOR GOVERNANCE OF EMERGING TECHNOLOGIES

Marc A. Saner and Gary E. Marchant*

ABSTRACT: This article provides a systematic checklist to guide proactive bilateral and international regulatory cooperation (in the sense of "alignment" or "harmonization") in the context of emerging technologies. The article is structured along a life-cycle starting with preregulatory activities and ending with postregulatory processes. The background research is based on a series of interviews with American and Canadian experts carried out in late 2013 as well as studies of previous international regulatory alignment examples. Our aim is to inform the regulatory debate on how to best develop proactively aligned regulatory programs for emerging technologies in bilateral (e.g., United States-Canada) and international contexts.

CITATION: Marc A. Saner and Gary E. Marchant, Proactive International Regulatory Cooperation for Governance of Emerging Technologies, 55 Jurimetrics J. 147–178 (2015).

2. *Develop Shared Working Definitions, Test Protocols and Standards*

Early adoption of consistent definitions, test protocols, and standards are a key step for subsequent alignment of national regulatory and policy approaches. If national definitions, protocols, or standards diverge or remain undecided, practices and approaches (e.g., data reporting and collection) built on those foundations may also diverge, making subsequent convergence more difficult. Inconsistent definitions result in significant confusion, inefficiency, and fragmentation, both within and between jurisdictions.[36]

3. *Engage Bilateral or Multilateral Senior Staff Formally and Regularly*

One of the most important, but perhaps underappreciated, mechanisms for promoting transnational regulatory alignment is regular meetings of senior staff (at least twice per year) from the cooperating nations to identify common issues, opportunities for alignment, data sharing issues, and early warning of potential problems warranting a coordinated response. Activities at these

WHO Drug Information Vol. 29, No. 1, 2015

Regulatory collaboration

The International Coalition of Medicines Regulatory Authorities (ICMRA)

A new global collaboration brings together senior leaders to provide coordinated, consistent, and strategic leadership in an increasingly globalized and complex regulatory environment. The International Coalition of Medicines Regulatory Authorities (ICMRA) is a voluntary, executive level entity that provides direction for a range of areas that are common to many regulatory authorities' missions.