

REGULATORY SCIENCE



Elias Zerhouni is President, Global R&D, Sanofi, Paris, France and former director of the U.S. National Institutes of Health, Bethesda, MD 20892, USA. Email: Elias.Zerhouni@sanofi.com



Margaret Hamburg is the Foreign Secretary of the U.S. National Academy of Medicine, Washington DC 20001, USA; former commissioner of the U.S. Food and Drug Administration (FDA), Silver Spring, MD 20993 USA; and former commissioner of the New York City Department of Health and Mental Hygiene, New York, NY 10013, USA. Email: Mhamburg@nas.edu

Citation:

E. Zerhouni, M. Hamburg, The need for global regulatory harmonization: A public health imperative. *Sci Transl Med*. 8, 338ed6 (2016).

10.1126/scitranslmed.aaf1396

CREDIT: MARTHE LEMELLE (E.Z.); SIMONS FOUNDATION (M.H.)

The need for global regulatory harmonization: A public health imperative

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 Stuff 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 comes at a time when many regulatory authorities are already struggling to keep up with rapid advances in science and technology as well as the growing complexity of medical products and product development, manufacturing, and supply. Additional pressures come from mounting economic and political desire to manage public spending and product costs.

In this context, we require a new strategic regulatory approach to ensure product safety, efficacy, and quality. Greater harmonization—coordination and alignment of regulatory rules—across nations would clearly benefit all stakeholders. So why has there not been more substantial global harmonization of essential regulatory activities such as product review, approval, labeling, supply-chain quality, and pharmaco-vigilance (which involves the postmarket monitoring of the effects of drugs)? Nations, of course, have sovereign approaches to legal-regulatory frameworks based on their own history, politics, and sociocultural values. The degree of acceptable risks and benefits, disease burden, vulnerable populations, privacy concerns, and the social and economic costs that vary across borders all can lead to regulatory divergence. Many regulators are also underresourced and struggle to acquire and maintain the necessary quality and number of experts to fully engage with stakeholders and keep pace with rapid advances in the volume and complexity of the products before them (2). Gaps in both the development of a unified body of regulatory science (3) and the availability of a well-trained regulatory workforce (4) also make global alignment more challenging.

In this world of growing public health needs, limited resources, and incessant demand for more, faster, cheaper, and better treatments, regulatory harmonization would have many benefits. Certainly, it could increase efficiencies and reduce costs, avoiding, for example, the duplication of effort when regulatory authorities perform overlapping reviews and inspections of clinical or manufacturing sites for similar purposes. Greater harmonization could enhance R&D, as discordant rules and regulatory approaches add significantly to the cost, complexity, and time needed to bring therapies to patients. A significant and rising portion of R&D budgets is spent

to satisfy differing regulatory requirements across countries for the same therapy directed to the same disease with no obvious added benefits—resources that could otherwise be spent on discovery. Most importantly, enhanced collaboration and coordination would benefit patients by ensuring that the best possible science, standards, and practice drive the regulatory process, resulting in improved safety, innovation, and access.

To their credit, regulatory authorities and their leaders are increasingly attuned to these concerns. Progress is being made and solutions sought. Regulatory authorities are working more frequently with each other, sharing inspection and safety information, and even conferring over discrete product approvals. Various bilateral and multilateral arrangements seek to enhance collaboration, learning, and sharing of best practices as well as efforts to strengthen the regulatory science that underlies regulation and oversight. Organizations such as the International Council on Harmonization (ICH), the Pharmaceutical Inspection Convention, and Pharmaceutical Inspection Co-operation Scheme (PIC/S) have proved valuable in establishing standards and guidelines for operational alignment across a range of nations. Of note, the International Coalition of Medicines Regulatory Authorities (ICMRA) is a recently established, voluntary leadership group at the highest levels (heads of medicines regulatory authorities) intended to create a broad, formal framework with which to enhance communication, collaboration, and regulatory alignment among regulatory authorities. Nevertheless, none of these entities have the authority to ensure, nor do any of these efforts promise, greater harmonized legislation that governs regulatory entities worldwide.

The need for more drug regulatory harmonization has never been greater—or more possible. Yet the nature of bureaucracy often maintains the status quo. Absent top-down impetus, transformation can be slow. Such seminal change needs to be driven by governments that recognize the advantages to linking arms and are willing to drive harmonization forward urgently. For almost all regulatory authorities—big and small, established or fledgling—greater commitment to regulatory systems and their harmonization at the senior political level is needed to redress unclear or missing legislative mandates as well as resource issues. There have been other such moments in innovation history, including with the railroad systems and civil aviation. In each of these cases, the risk of disharmonization was evident, with well-publicized cases of accidents and near misses, such that the imperative to align across borders to protect consumers became a *cri de coeur*.

The regulation of drugs can either grease the wheels of progress or throw a wrench in the works. We believe that harmonized drug regulation has the potential to be the unsung hero in driving improved health along with global economic and social development. We would challenge governments, including congresses and parliaments, presidents and prime ministers, to put harmonization on their agendas and those of the G-8 or G-20 as a critical and transformative next step in advancing public health for all.

—Elias Zerhouni and Margaret Hamburg

REFERENCES

1. J. P. Griffin, Venetian treacle and the foundation of medicines regulation. *Br. J. Clin. Pharmacol.* **58**, 317–325 (2004).
2. New realities of globalization. <http://www.fda.gov/NewsEvents/Speeches/ucm388388.htm>.
3. R. B. Altman, N. Khuri, M. Salit, K. M. Giacomini, Unmet needs: Research helps regulators do their jobs. *Sci. Transl. Med.* **7**, 315ps22 (2015).
4. C. Skarke, G. A. FitzGerald, Training translators for smart drug discovery. *Sci. Transl. Med.* **2**, 26cm12 (2010).

Science Translational Medicine

The need for global regulatory harmonization: A public health imperative

Elias Zerhouni and Margaret Hamburg

Sci Transl Med **8**, 338ed6338ed6.
DOI: 10.1126/scitranslmed.aaf1396

ARTICLE TOOLS <http://stm.sciencemag.org/content/8/338/338ed6>

RELATED CONTENT <http://stm.sciencemag.org/content/scitransmed/8/335/335ps10.full>
<http://stm.sciencemag.org/content/scitransmed/7/315/315ps22.full>
<http://stm.sciencemag.org/content/scitransmed/6/252/252cm7.full>
<http://stm.sciencemag.org/content/scitransmed/8/333/333ps8.full>
<http://stm.sciencemag.org/content/scitransmed/7/296/296ed9.full>
<http://stm.sciencemag.org/content/scitransmed/4/163/163fs43.full>
<http://stm.sciencemag.org/content/scitransmed/4/150/150fs35.full>
<http://stm.sciencemag.org/content/scitransmed/8/347/347ed10.full>

REFERENCES This article cites 3 articles, 2 of which you can access for free
<http://stm.sciencemag.org/content/8/338/338ed6#BIBL>

PERMISSIONS <http://www.sciencemag.org/help/reprints-and-permissions>

Use of this article is subject to the [Terms of Service](#)

Science Translational Medicine (ISSN 1946-6242) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. The title *Science Translational Medicine* is a registered trademark of AAAS.

Copyright © 2016, American Association for the Advancement of Science