Regulatory Science in 2017

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A series of significant trends have marked the global regulatory landscape in 2017.

Common themes related to questions of how to

- effectively use Artificial Intelligence (AI) in the regulatory process, such as natural language programming;
- develop Real World Evidence (RWE) standards and validation tools to use patient data constructively and accurately;
- meet ICH (International Council for Harmonisation) training needs to ensure compliance with the growing number of ICH guidelines; and
- avert prescription drug abuse.

Steps to expand globally harmonized regulatory processes have received particular attention. China became an important new member of ICH this year, and several countries and regions agreed to new ICH mandates and entered mutual agreements:

- The ICH E6(R2) Guideline for Good Clinical Practice (GCP) provides the EU, Japan, and the US with a unified standard for compiling study reports and managing data, enabling regulatory authorities in these regions to accept each other's clinical data.
- Experts from different regions and organizations revised their newly drafted ICH MRCT Guideline (E17) that outlines standards for planning and designing Multi-Regional Clinical Trials (MRCTs) intended for submissions to multiple regulatory authorities. The draft was recently finalized and is expected to make new medicines more rapidly available to patients worldwide.
- The US and EU entered a Mutual Recognition Agreement (MRA) on good manufacturing practice (GMP) inspections to streamline and harmonize safety inspections across the Atlantic. Once the MRA is fully implemented, inspectors of either region will no longer need to duplicate their efforts, enabling regulators to devote more resources to other parts of the world.

In addition to these commonalities, each region also dealt with a few hot topics of their own.

Americas

In the US, discussions revolved around the 2017 FDA Reauthorization Act (FDARA), the US generic drug review program and the 21st Century Cures Act, and how to make the approval process more efficient, especially with regard to therapies for rare diseases. The FDA also made headway in addressing the opioid crisis and in advancing a mutual drug inspection agreement with the EU (see above).

FDARA reauthorized the Prescription Drug User Fee Act (PDUFA VI), the Medical Device User Fee Amendments (MDUFA), the Generic Drug User Fee Amendments (GDUFA), and the Biosimilar User Fee Act (BsUFA). Building on the goals of the 21st Century Cures Act and previous user fee agreements, the law

- enhances FDA's ability to capture the patient voice in drug development;
- facilitates the development and timely approval of drugs and biologics for rare diseases;
- advances generic drug and biosimilar approvals, improving patient access to safe, affordable treatments (GDUFA and BsUFA); and
- encourages the use of Real World Evidence (RWE) to inform regulatory decision-making and support premarket activities.

To address the wave of opioid misuse and abuse that has swept the US and balance the risks with the need for approved opioids, the FDA:

- Has issued letters to manufacturers of immediate-release (IR) opioid analgesics whose drugs will now be subject to more stringent criteria under a Risk Evaluation and Mitigation Strategy (REMS);
- Will expand the current REMS to include content on the safe use of opioids, opioid use disorders, pain management, and non-opioid alternatives;
- Will release a final guidance to help applicants with approval applications for generic versions of abuse-deterrent formulations (ADFs) of opioid drugs, such as Extended-Release/Long-Acting (ER/LA) opioids; and
- Plans to make training available to health care professionals involved in the management of patients with pain.

After consultations with various stakeholders, Canada proposed to amend drug pricing regulations that govern the Patented Medicine Prices Review Board (PMPRB), which protects consumers from excessive drug prices. The proposed amendments reduce the regulatory burden for generic manufacturers and equip the PMPRB with new tools to evaluate drug prices, including a much longer list of country comparators.

In South America, Mercosur, an important player in the trade and regulatory affairs arena, has refocused its attention on economic and commercial issues. The Cooperation and Investments Facilitation Protocol was signed last April, providing legal protection to investors across participating countries in Latin America. Solutions for an integrated healthcare market in Latin America are among Mercosur's other priorities.

The regulatory landscape in Brazil was also marked by a few other developments:

- Stakeholders have pushed for reform of the current regulatory framework that would foster a friendlier regulatory environment for clinical trials.
- Law n.13411/2016 established new deadlines for regulatory review of new drug and post-approval applications by the Brazilian National Health Surveillance Agency (ANVISA), and defines "priority submissions" versus "ordinary submissions."

Asia

Since 2015, the China Food and Drug Administration (CFDA) has steadily implemented a series of wide-ranging reforms to its regulatory framework, culminating in the CFDA becoming a Regulatory Member of the International Council for Harmonization (ICH) in June 2017. As part of China's sweeping reforms, the State Council and the Communist Party's Central Committee in October 2017 issued policy reforms and guidelines to overhaul the country's healthcare product development and approval process. The goal is to promote the development of innovative drugs and medical devices by improving clinical trial management, expediting reviews, and allowing clinical trial data from other countries to be used for approval in China. China's new reforms will also improve the quality of generic drugs.

Japan, a country that has long focused on regenerative medicine, has begun to allow the use of the first cell therapy products, a move that has sparked discussions with government and scientific authorities on issues related to quality control, development, and marketing that are unique to these products.

The ICH Training Subcommittee recently approved the first regional ICH training in ASEAN as part of its effort to partner with experienced trainers in different regions to provide ICH training worldwide.

Europe

The current environment for clinical research and regulatory science in Europe has brought about several interesting developments in 2017. And with the UK's vote to withdraw from the European Union (Brexit), Europe is facing a unique set of challenges and consequences:

- The EU Medical Devices Regulation (MDR) and in Vitro Diagnostic Regulations (IVDR) provides a new regulatory framework with centralized controls on high-risk medical devices, requiring that devices already on the market be re-assessed.
- Healthcare professionals are implementing the new clinical trial data transparency framework.
- Regulatory science professionals are discussing how artificial intelligence (AI) and other new tools can improve drug development.
- In collaboration with the Netherlands, EMA strives to keep disruptions to its operations to a minimum while its headquarters relocate to Amsterdam.
- EMA's Brexit Preparedness Business Continuity plan is due to begin in January 2018.

Other

In India, pharmacovigilance-specific cognitive computing applications are being considered for case processing operations that are needed to fulfill regulatory requirements but can be resource-intensive if performed manually.

The Australian Pharmaceutical Benefits Advisory Committee (PBAC) and Therapeutic Goods Administration (TGA) jointly introduced two new TGA registrations pathways to avoid overlaps in the assessments of medicinal products: Priority Review for new medicines that already come with a full data dossier from another registration authority, and Provisional Approval for new medicines that still lack sufficient clinical data.

The African Vaccines Regulatory Forum (AVAREF) developed proposals to streamline the regulation of clinical trials on the continent.

There will be more competition between the US and EU in their race to gain experience and approve biosimilars, potentially speeding up the approval process. Streamlined regulations for generics, on the other hand, may proceed less quickly as everyone sorts out how to address pediatric versions.

WHAT LIES AHEAD?

"China becoming an integral part of the ICH can only improve the safety, efficacy, and quality of products produced in the region at a time when cost containment in the US is becoming more critical and political. This will allow China to gain on India's lead, if India does not focus similarly on higher quality standards for production. The question is whether this will encourage generic and biosimilars to be sourced in China, especially if the revised US tax code will not be incentive enough to bring companies back to the US."

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