Plenary 5: Improving regulatory capacities

Innovative Pharmaceutical Development Approaches require strong Regulatory Systems – An Industry Perspective

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A reality for many regulators/NRAs – also in LATAM

What would you do?

You are the HEAD of an NRA in a low-income country, and you have **20 regulatory staff**.

You receive ~300 applications per year, of which < 10 are for new innovative medicines, you have **2 local manufacturers with** only 20 essential medicines registered out of 2,200 registered products, population of **3 million people**, **98.5%** are imported medicines.
Science is evolving and many promising new modalities and medicines are expected to reach NRAs soon

**CAR-T therapies** – are T-cells that have been genetically modified to allow the T-cell to recognize and destroy tumor cells

**Combination therapies** – increasing quality and quantity of life by combining targeted cancer treatments to increase their effectiveness

**Gene therapy** – helping to replace defective or missing genes in cells through the introduction of DNA for the treatment of genetic diseases

**Cell therapy** – insertion of living cells into patients to replace or repair damaged tissue, in order to facilitate improved organ or tissue functionality

**Antibacterial treatments** – neutralize highly pathogenic bacterial surface proteins or secreted toxins and activate the immune system to directly kill the bacteria

With over 7000 medicines in development, the exciting new wave of medical innovation will play a key role in addressing the challenges faced by patients and healthcare systems

Adapted from “Health Advances analysis; Adis R&D Insight Database. March 2015, compiled by PhRMA”
Science and technology are shifting the boundaries of what is possible in medical research and patient care

**Methodologies**

- Biomarker-guided Clinical Trial Designs
  - Basket trials
  - Umbrella trials
- Adaptive Designs

**Major Goals**

- Increase R&D efficiency
- Increase the number of trial participants getting the best treatment
Innovative drug development approaches require innovative and strong regulatory systems and procedures

Consequences

• Smaller Patient Numbers
• Faster Development Timelines
• Tighter (more specific) Clinical Experience

• Shift of some traditional pre-approval development activities into the post-approval space

Enablers

• Accelerated Approval Pathways
  • Rolling Submissions
  • Parallel Companion Diagnostics (CD) Evaluation
  • Post-Approval Commitments
  • CMC-Flexibility

• Reliance Options
  • Recognition
  • Verification
  • Abbrided

• Robust Pharmacovigilance System
• Efficient Life-Cycle Management

PAHO
Accelerated Approval Pathways:
Regulatory pathways/components that should be available in an up-to-date regulatory system accelerating regulatory decision making for products addressing unmet medical needs.

Source: EFPIA White paper on reliance and expedited registration pathways in emerging markets, 2017
Robust Pharmacovigilance System: Proper Safety Surveillance (PV) still a dream in most countries but WHO Triple-S principles may provide a way forward
Implementation of highly elaborated WHO-guidance may easily solve many issues around achieving efficient product life-cycle management (LCM)

E.g. the WHO post approval change guidance for biotherapeutic products* (BTPs) has all features that will significantly facilitate the work related to product life-cycle both at industry and NRAs including:

- state-of-the-art risk-assessments
- change categorization based on experience
- data requirements ensuring proper risk-mitigation
- timelines that lead to predictable implementation
- recognition and reliance based evaluation procedures

The almost 70 examples provided in the guidance on CMC related Drug Substance and –Product changes cover approx. 90% of the changes that are frequently made for BTPs (“Check-List”)

It should be implemented in each LATAM country!!

*WHO Guidelines on post approval changes for biotherapeutic products Appendix 1
While we see encouraging examples and results of regulatory systems strengthening efforts in the region like:

- **establishment and implementation of regulations for biologics** now in almost all countries across the region
- A well functioning **CRS as the flagship for collaborative regulatory decision making** in LATAM that may serve as an example for others
- **Implemented and piloting reliance based regulatory pathways** e.g. Panama and Brazil

In many LATAM countries there is still need for:

- Engagement in the **development and implementation of alternative registration pathways** for products addressing unmet need e.g. through FDA mentoring
- Applying principles of Good Regulatory Practice by **piloting, adopting and executing reliance based procedures in regulatory decision making** e.g. it may be helpful to develop procedural guidance on how to practically implement reliance concepts
- Driving robust **pharmacovigilance system implementation along WHO Triple-S principles** to ensure patient safety
- Continued **alignment and establishment of local regulatory requirements along global standards** and best practices (ICH/WHO/PICS/etc.) e.g. WHO post-approval guidance for BTPs and vaccines to be translated by PAHO
Fragmentation, duplication and inefficiency are undermining progress.

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So we have choice: we can keep doing what we’re doing. But we must accept that the outcomes will be the same. Let me remind you that the definition of insanity is to keep doing the same thing and expect a different result. We must do something different.
We need innovation and disruption – not just for developing new products, but for developing new ways of delivering those products and new ways of working together to deliver results.

From: Opening speech for the World Health Summit, Dr Tedros Adhanom Ghebreyesus, WHO Director-General, Berlin, Germany 16 October 2018