Plenary 5: Improving regulatory capacities

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

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On behalf of FIFARMA

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

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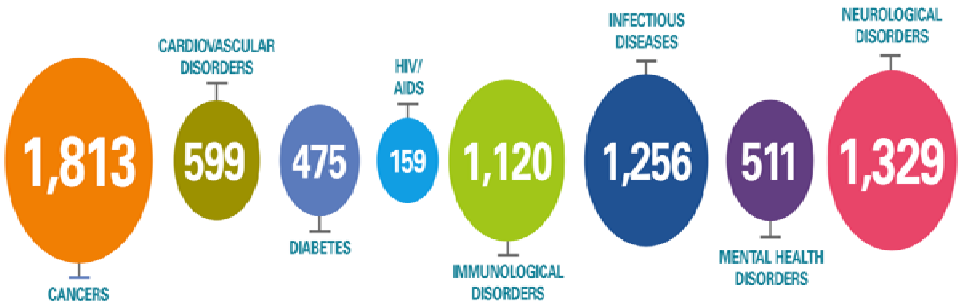
With **over 7000 medicines in development**, the exciting new wave of medical innovation will play a key role in **addressing the challenges faced by patients and healthcare systems**



Adapted from "Health Advances analysis; Adis R&D Insight Database. March 2015, compiled by PhRMA'

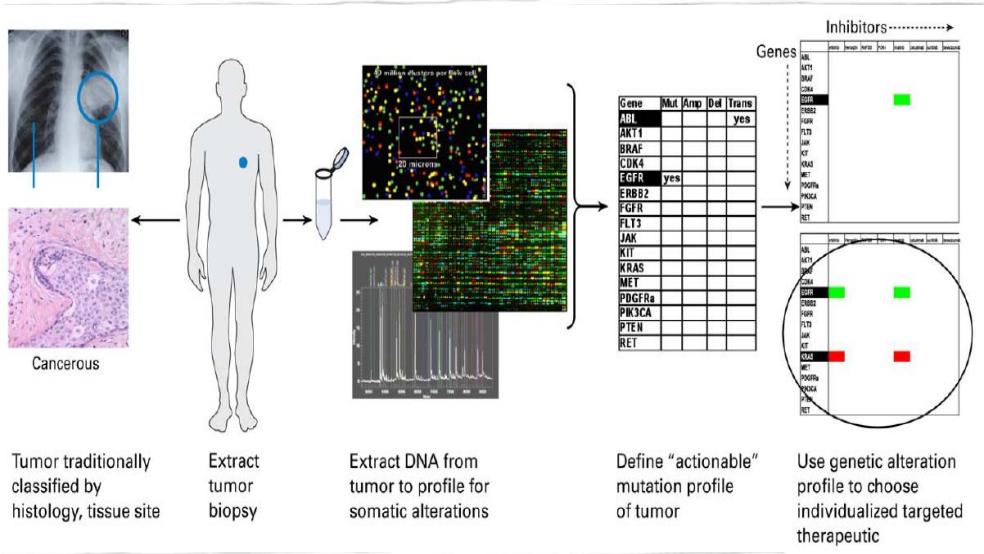
Science and technology are shifting the boundaries of what is possible in medical research and patient care

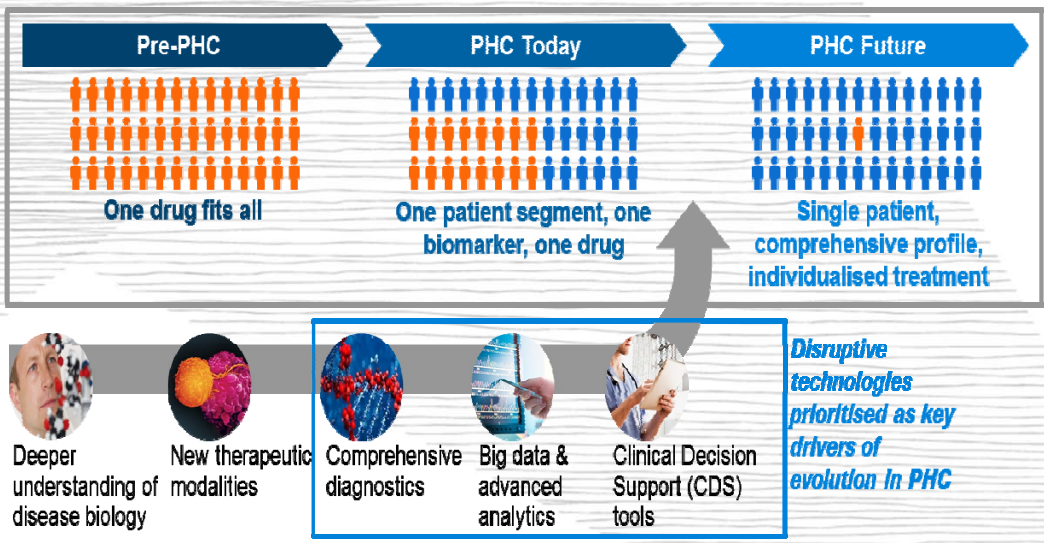
Methodologies

- 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 Committments
  - CMC-Flexibility
- **Reliance Options**
  - Recognition
  - Verification
  - Abbridged
- **Robust Pharmacovigilance System**
- **Efficient Life-Cycle Management**

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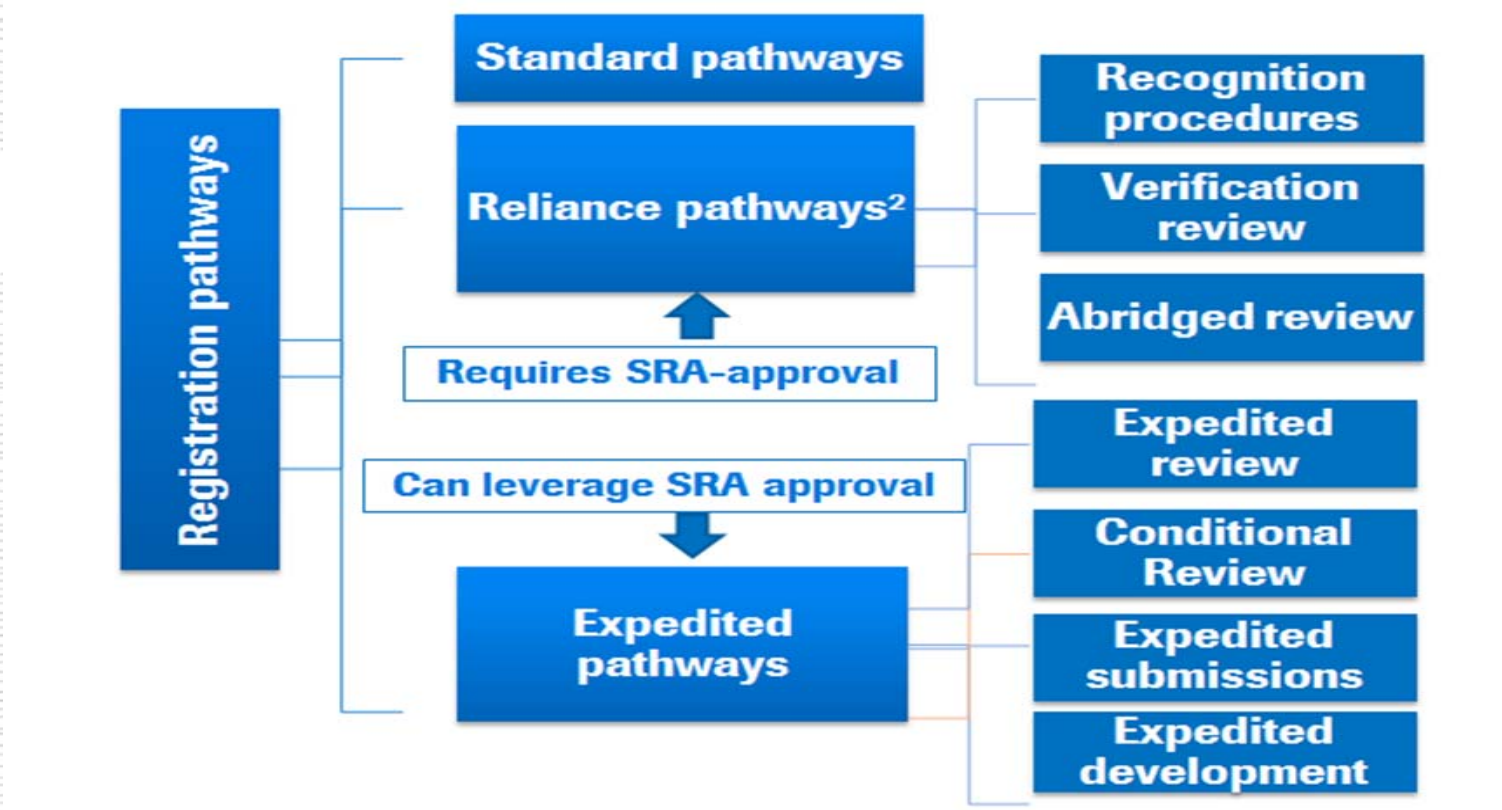
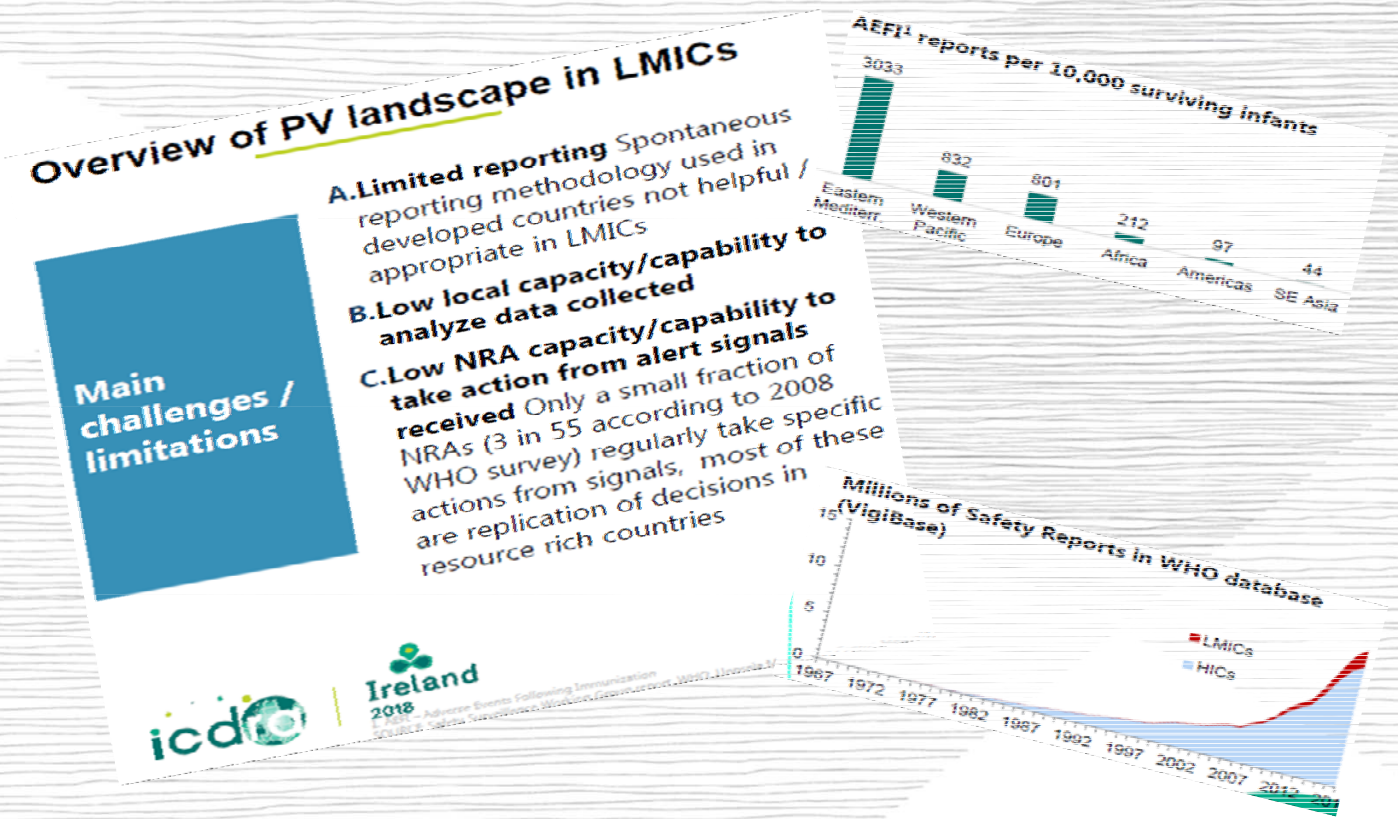
Accelerated Approval Pathways:
Regulatory pathways/components that should be available in an up-to-date regulatory system accelerating regulatory decision making for products addressing unmet medical needs



Source: EFPIA White paper on reliance and expedited registration pathways in emerging markets, 2017
https://www.efpia.eu/media/288592/white-paper-on-reliance-and-expedited-registration-pathways-in-emerging-markets.docx

Robust Pharmacovigilance System:
Proper Safety Surveillance (PV) still a dream in most countries but WHO Triple-S principles may provide a way forward



Pilot products: Adopt a stepwise approach with an initial pilot for three new products (two medicines and one vaccine)

Holistic country plan: Develop a holistic plan for pharmacovigilance as part of medicines regulation in the defined countries

Industry partnership: Develop integrated plans that include key marketing authorization holders

Leverage available resources from partners: WHO International Drug Monitoring Programme, Global Vaccine Safety Initiative, Uppsala Monitoring Centre and other WHO collaborating centres, national pharmacovigilance centres and others

Progressive development: Build pharmacovigilance infrastructure progressively, moving from minimum to mid-range and advanced capacity.

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Adapted from Summary Plenary 1 «Smart Safety Surveillance» pre-ICDRA Dublin, 2018

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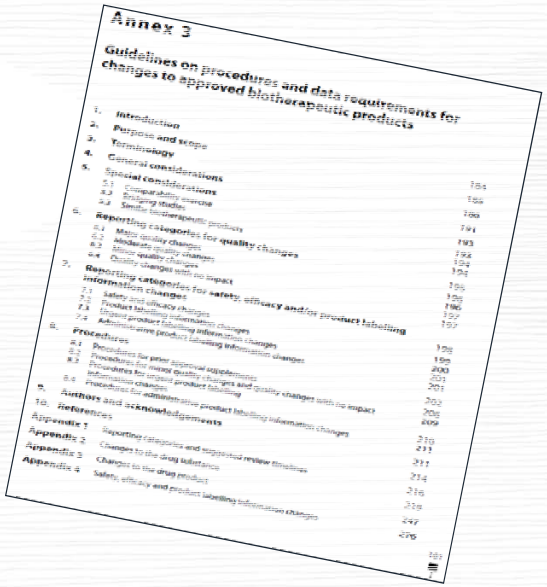
Implementation of highly elaborated WHO-guidance may easily solve many issues around achieving efficient product life-cycle management (LCM)



Annex 3

Guidelines on procedures and data requirements for changes to approved biotherapeutic products

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

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FIFARMAs asks for PAHO and NRAs:

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

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Fragmentation, duplication and inefficiency are undermining progress.

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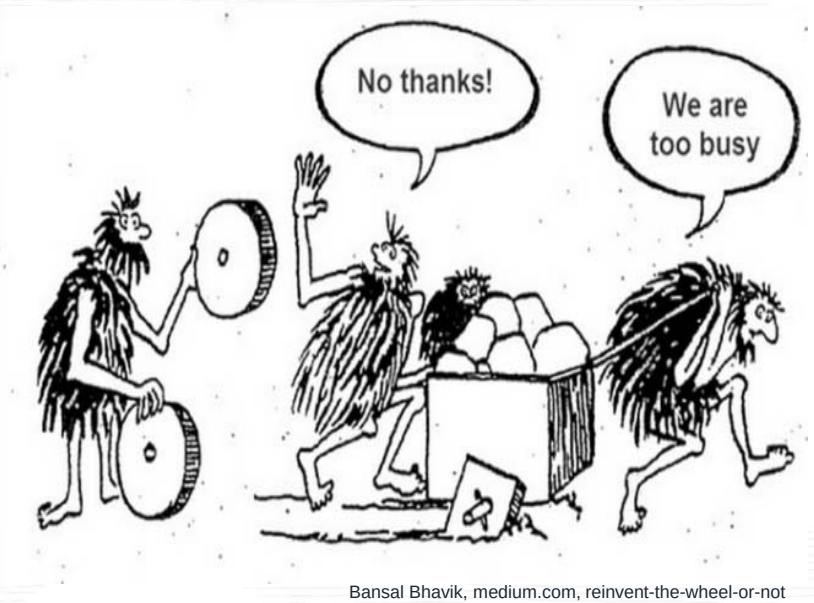
So we have choice: we can keep doing what we're doing. But we must accept that the outcomes will be the same.

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



Bansal Bhavik, medium.com, reinvent-the-wheel-or-not

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