

## 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.

WHO/HIS/EMP | March 17, 2017, Mike Ward



World Health Organization



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# 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

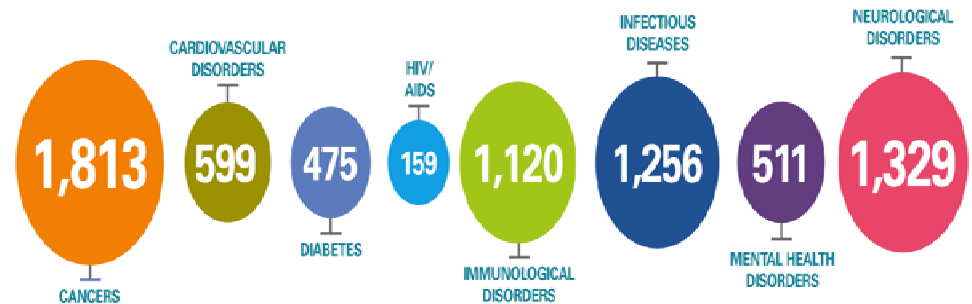


**Cell therapy** – insertion of living cells into patients to replace or repair damaged tissue, in order to facilitate improved organ or tissue functionality



**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"

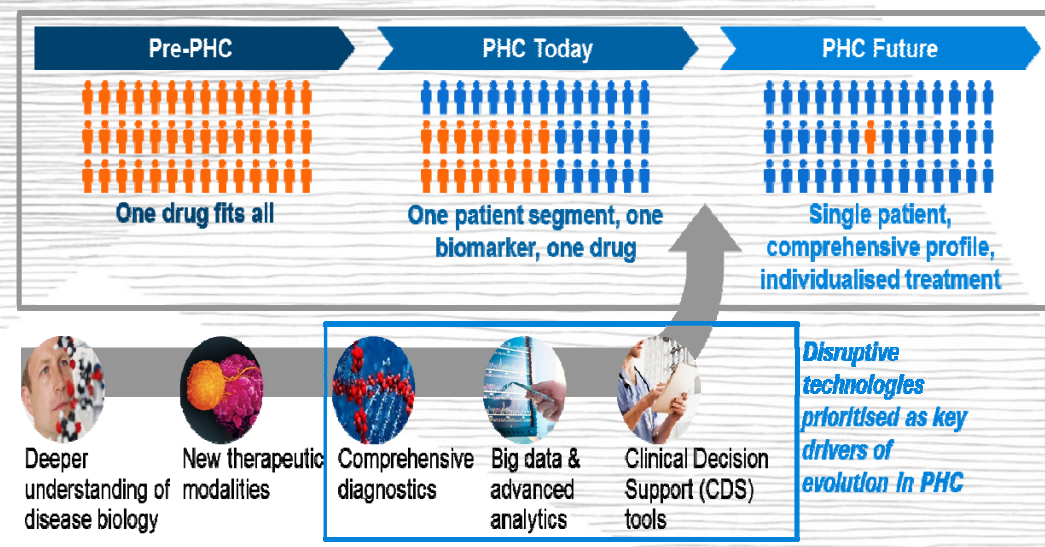
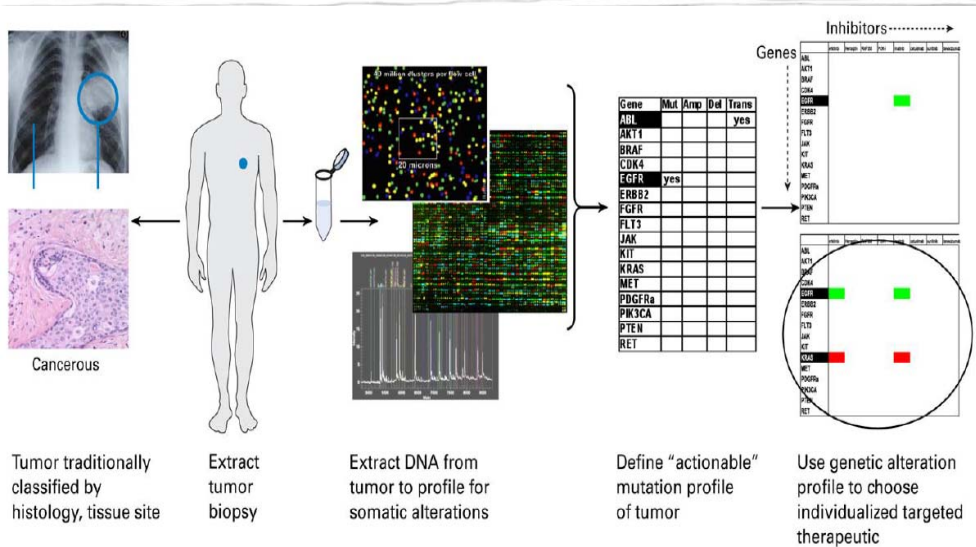
# Science and technology are shifting the boundaries of what is possible in medical research and patient care

## 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

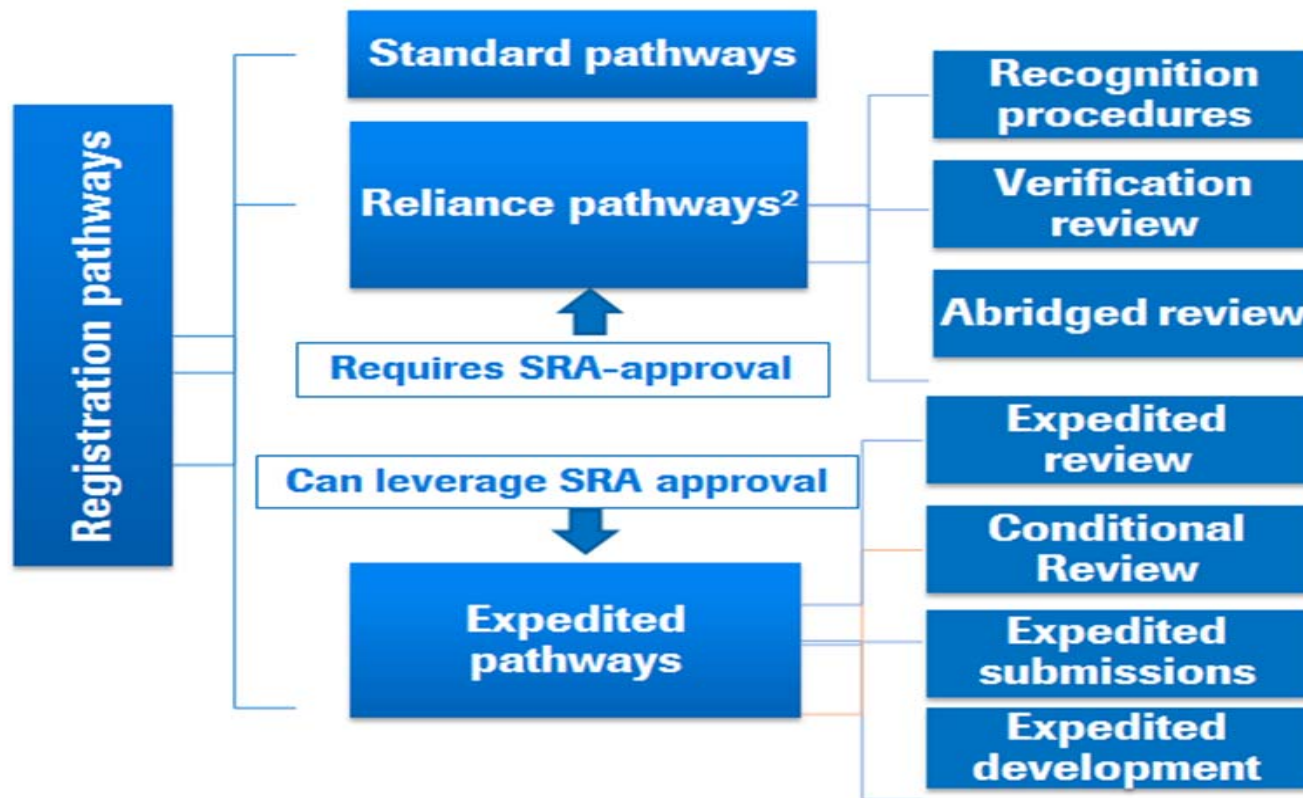
- **Smaller** Patient Numbers
- **Faster** Development Timelines
- **Tighter** (more specific) Clinical Experience
  
- **Shift of some traditional pre-approval development activities into the post-approval space**

## Enablers

- **Accelerated Approval Pathways**
  - Rolling Submissions
  - Parallel Companion Diagnostics (CD) Evaluation
  - Post-Approval Commitments
  - CMC-Flexibility
- **Reliance Options**
  - Recognition
  - Verification
  - Abbridged
- **Robust Pharmacovigilance System**
- **Efficient Life-Cycle Management**

## 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>



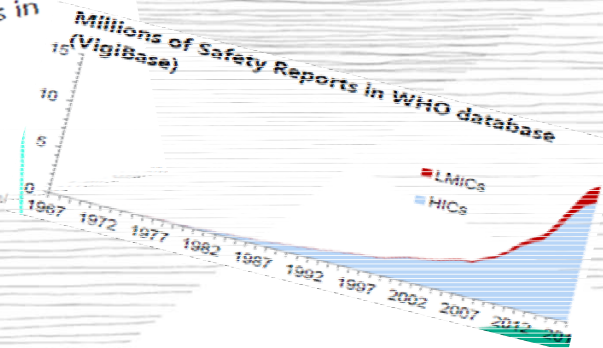
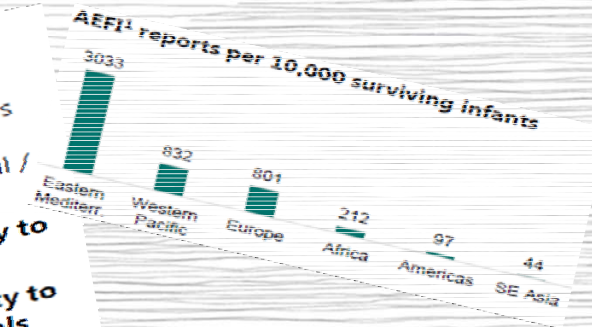
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# Robust Pharmacovigilance System: Proper Safety Surveillance (PV) still a dream in most countries but WHO Triple-S principles may provide a way forward

## Overview of PV landscape in LMICs

### Main challenges / limitations

- A. Limited reporting** Spontaneous reporting methodology used in developed countries not helpful / appropriate in LMICs
- B. Low local capacity/capability to analyze data collected**
- C. Low NRA capacity/capability to take action from alert signals received** Only a small fraction of NRAs (3 in 55 according to 2008 WHO survey) regularly take specific actions from signals, most of these are replication of decisions in resource rich countries



**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.

WHO Drug Information Vol. 31, No. 4, 2017

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

## 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 biotechnological 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 !!

**Annex 3**  
**Guidelines on procedures and data requirements for changes to approved biotechnological products**

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\*WHO Guidelines on post approval changes for biotechnological products Appendix 1



## 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

*Fragmentation, duplication and inefficiency are undermining progress.*

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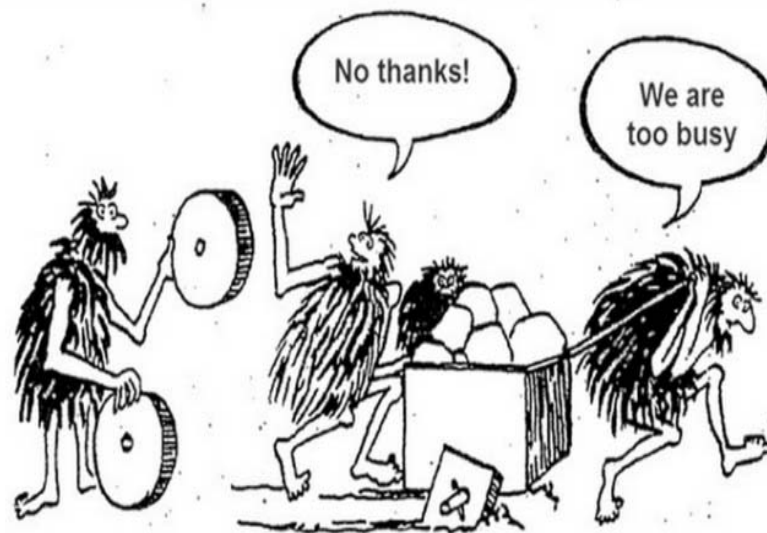
*So we have choice: we can keep doing what we're doing. But we must accept that the outcomes will be the same.*

*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