

# Pharmacovigilance in low- and middle-income countries (LMICs)

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*Team Lead*

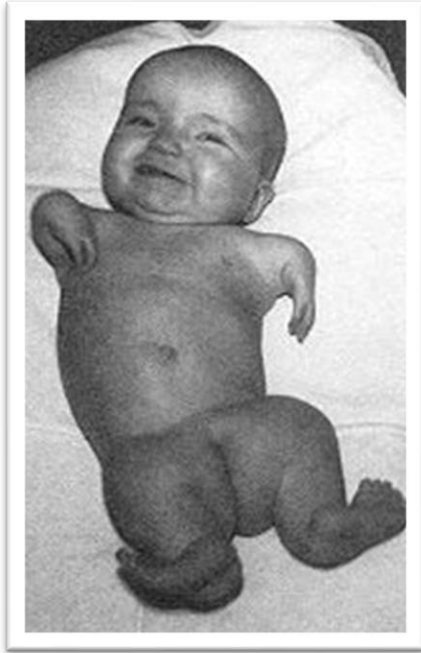
*Pharmacovigilance*

*WHO*



# The foundation of the WHO PVG Programme

- After the thalidomide disaster

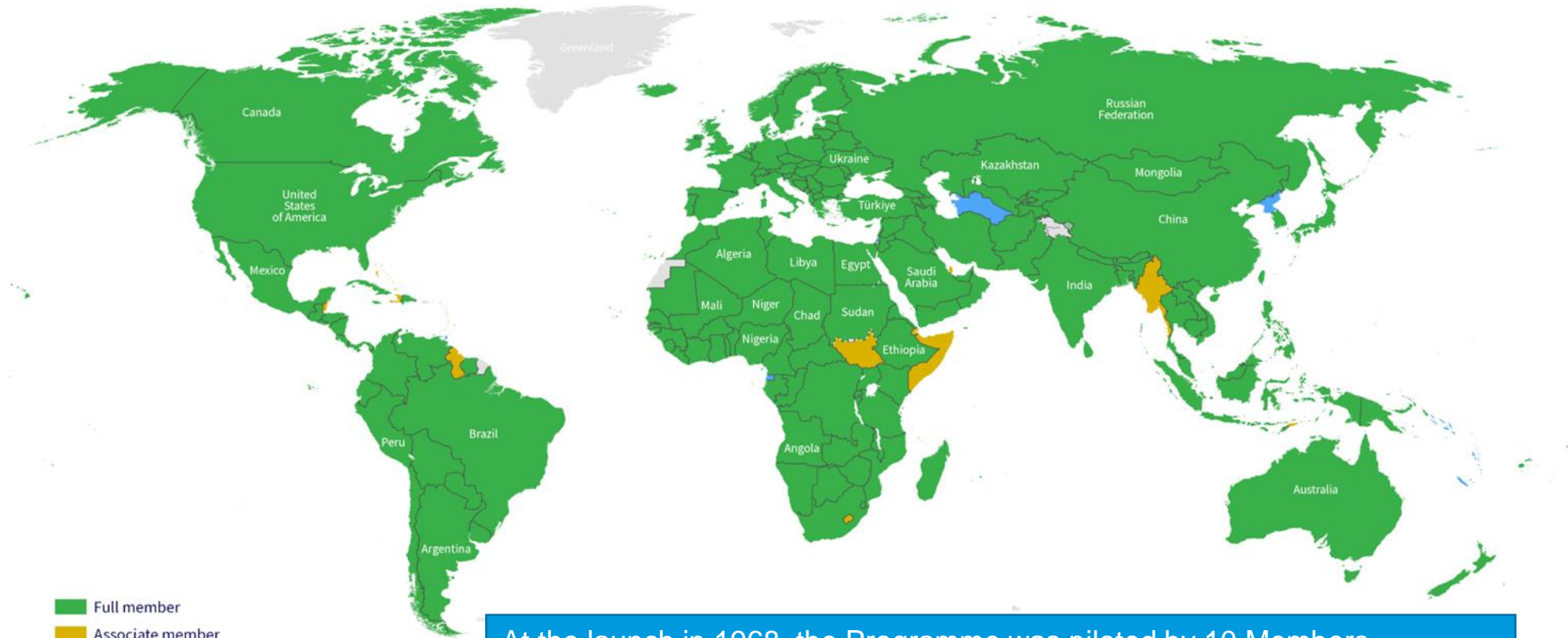
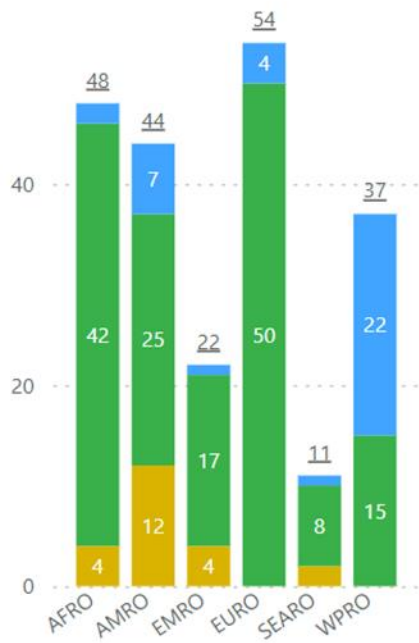
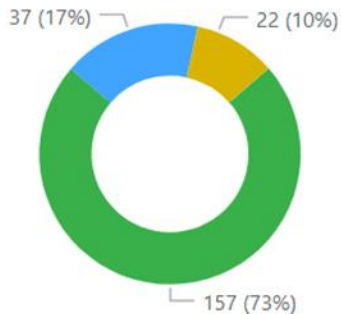


Thalidomide – children born 1957 - 1963

In 1963, during the 16th World Health Assembly, resolution 16.36 called for “a *systematic collection of information on serious adverse drug reactions during the development and particularly after medicines have been made available for public use*”.



**The WHO Programme for International Drug Monitoring (PIDM) was established in 1968.**



At the launch in 1968, the Programme was piloted by 10 Members.

179 Members in the Programme as of 27 March 2024.  
(157 Full and 22 Associate)

0 1000 2000 4000 km

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Data Source: WHO UNICEF eJRF

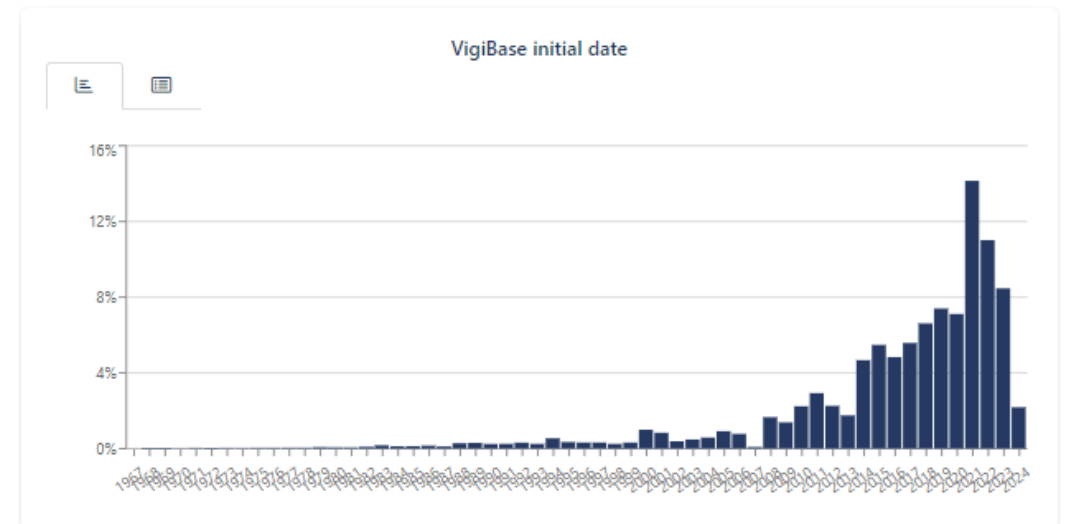
Map Creation Date: **11 April 2024**

Map Production: WHO GIS Centre for Health, DNA/DDI

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# VigiBase

- VigiBase is **the unique WHO global database of reported adverse events of medicinal products**. VigiBase is technically maintained by the WHO Collaborating Centre, Uppsala Monitoring Centre (UMC).
- It is the largest database of its kind in the world, with Individual Case Safety Reports (ICSRs) submitted since 1968, by Members of the WHO PIDM.
- It is continuously updated with incoming reports. **As of mid-April 2024, more than 150 Members shared approx. 37,900,000 ICSRs with VigiBase.**

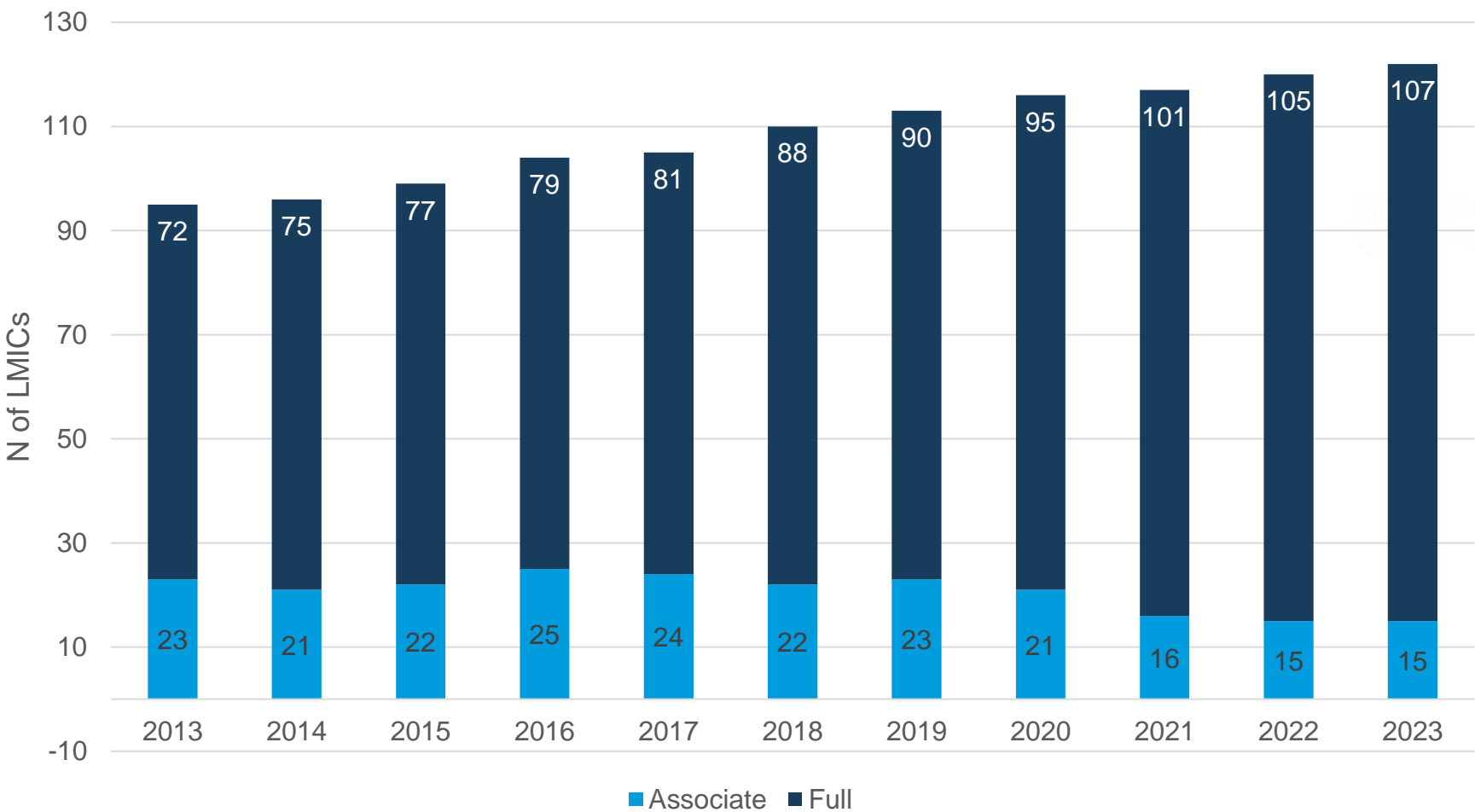


Searched on 16 April 2024

# Number of LMICs in the WHO Programme for International Drug Monitoring (PIDM)



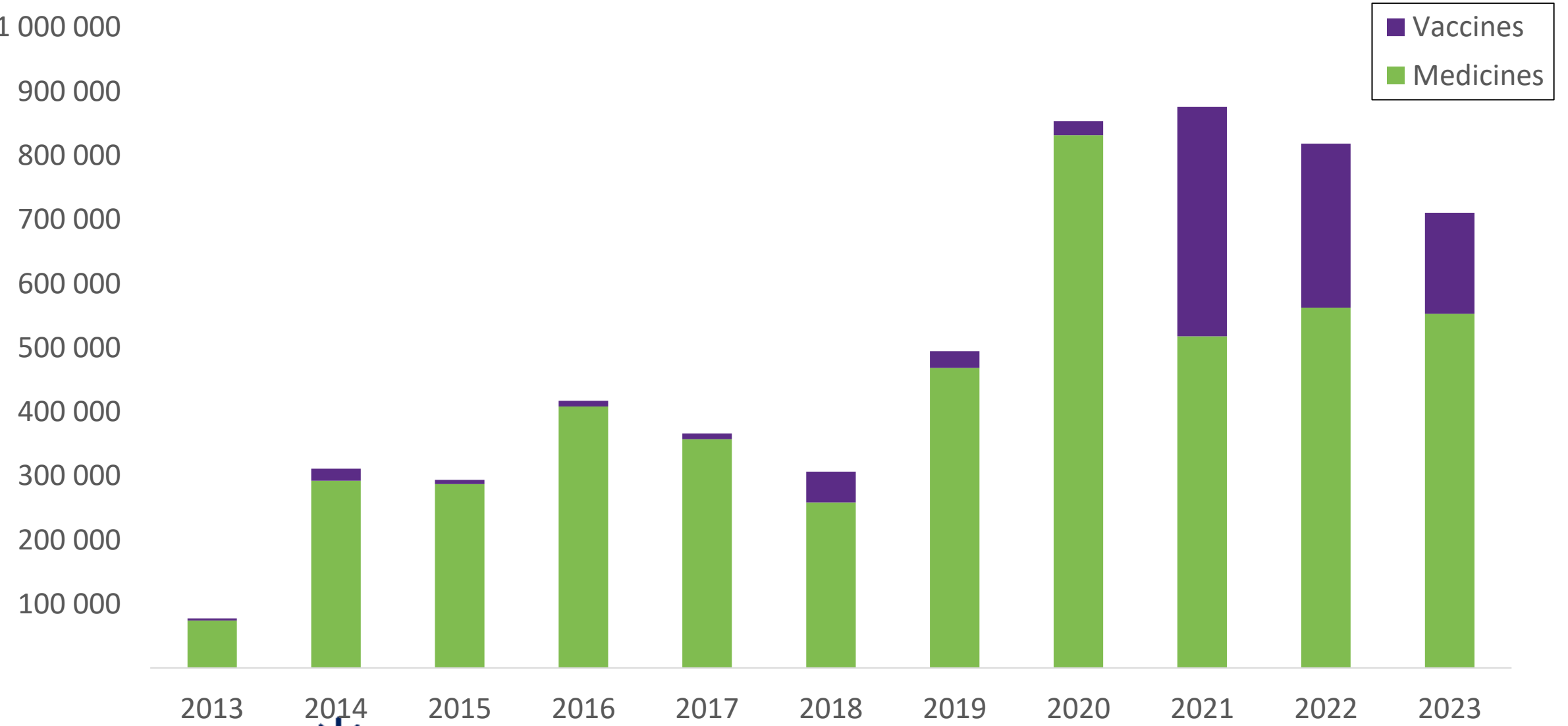
Evolution over time



Note: Indicated data are as of the end of each year from 2013 to 2022 and as of the end of October for 2023.

Reference: The WHO PIDM Internal Database, World Bank Country and Lending Groups ([URL](#))

# Number of ICSRs reported by LMICs 2013-23 (N ≈ 5.5 million)

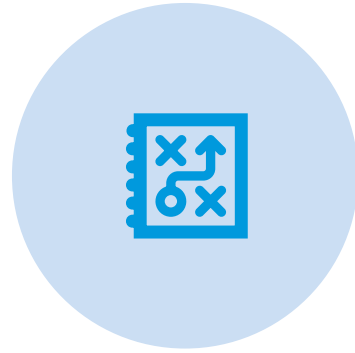


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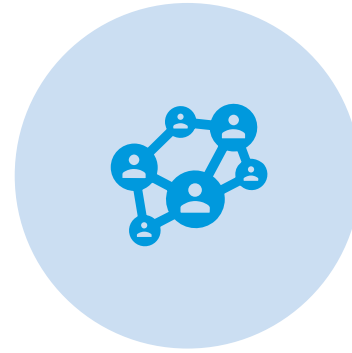
# 4 pillars underpin the WHO Pharmacovigilance Strategy



**LEARNING ON LEARNINGS**



**STRATEGIC SHIFTS**



**SYSTEM  
STRENGTHENING-  
TIERED, STEP-WISE  
APPROACH**



**RISK-BASED  
PRIORITIZATION**



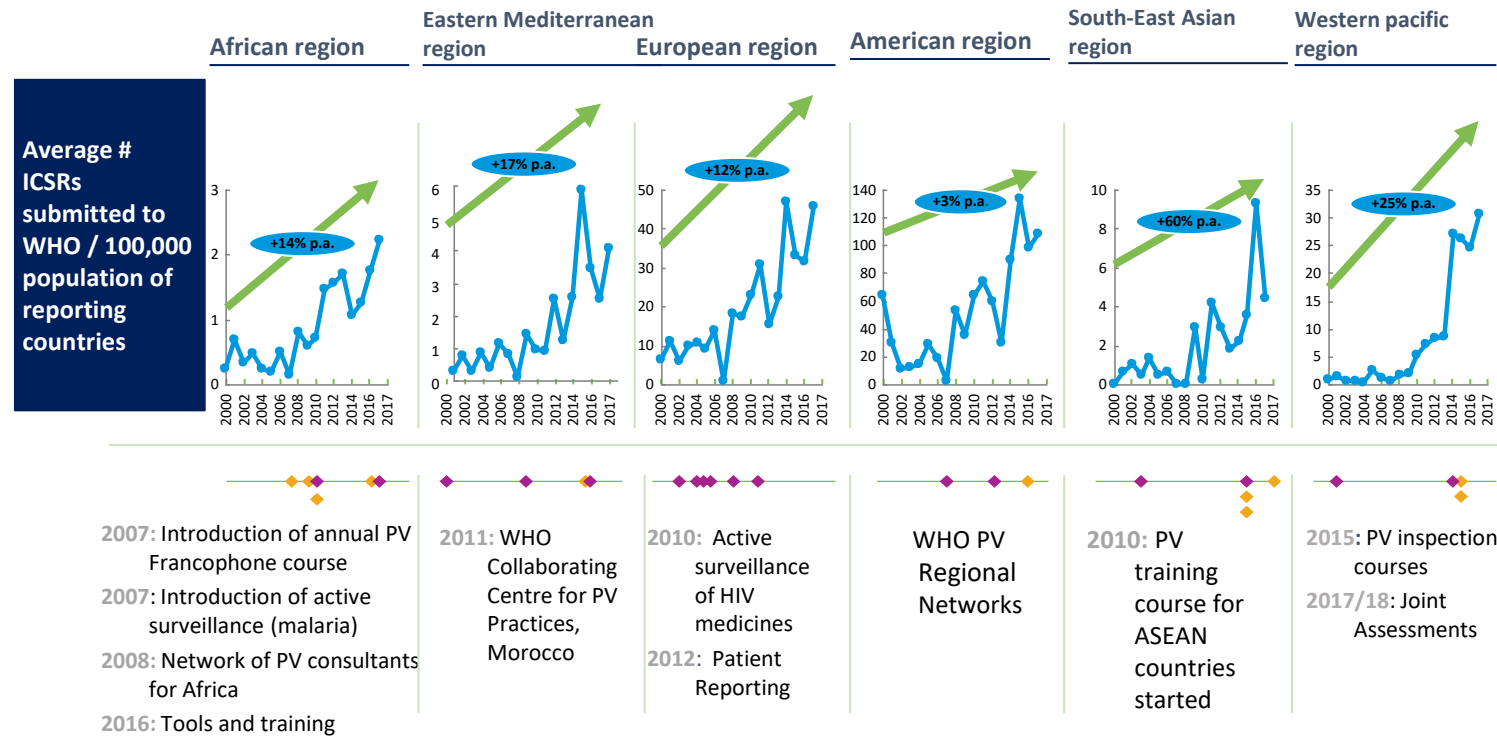
World Health  
Organization



HEALTH  
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## Leaning on Learnings

Number of reports on adverse events with medicines



◆ Annual meetings hosted in rotation by regions

2008: Affordable PV data management system developed for LMICs  
2010: WHO-Global Fund decision to include Min PV in GF grants;  
2011: WHO ISoP PV Curriculum Developed

SOURCE:WHO global database of ICSRs (Vigibase)

# One Size Doesn't Fit All: Strategic Shifts in How We Engage with Countries

Key Themes of WHO's 13<sup>th</sup>  
Draft General Programme of  
Work 2019-2023

**“Together for  
a healthier world”**

Dr Tedros Adhanom Ghebreyesus

Director-General



**Mission**

**Promote Health - Keep the World Safe - Serve the Vulnerable**

**Strategic  
Priorities**

**Health Coverage:** 1 billion more people with health coverage  
**Health Emergencies:** 1 billion more people made safer  
**Health Priorities:** 1 billion lives improved

**Strategic Shifts**

**Set up global  
leadership**

**Drive impact in every country**

Policy dialogue Strategic support Technical assistance Service delivery

← Mature health system

→ Fragile health system

**Focus  
global  
public  
goods on  
impact**

# Number of LMICs in ICH (as of June 2023)



- There are 21 Members in ICH, of which **five regulatory authorities are of LMICs**:
  - **Founding Members:**
    - Founding Regulatory Members: EC, Europe; MHLW/PMDA, Japan; FDA, United States
    - Founding Industry Members: EFPIA; JPMA; PhRMA
  - **Standing Regulatory Members:** Health Canada, Canada; Swissmedic, Switzerland
  - **Regulatory Members:** ANVISA, Brazil; COFEPRIS, Mexico; HSA, Singapore; MFDS, Republic of Korea; MHRA, UK; NMPA, China; SFDA, Saudi Arabia; TFDA, Chinese Taipei; TITCK, Turkey; EDA, Egypt
  - **Industry Members:** BIO; Global Self-Care Federation; IGBA
- There are 36 Observers in ICH, of which **19 regulatory authorities are of LMICs**:
  - **Standing Observers:** IFPMA; WHO
  - **Legislative Authorities:** AEC, Azerbaijan; ANMAT, Argentina; ANPP, Algeria; CDSCO, India; CECMED, Cuba; CPED, Israel; DPM, Tunisia; Indonesian FDA; Indonesia; INVIMA, Colombia; JFDA, Jordan; MMDA, Moldova; MOPH, Lebanon; National Center, Kazakhstan; NPRA, Malaysia; NRA, Iran; Roszdravnadzor, Russia; SAHPRA, South Africa; SCDMTE, Armenia; SECMOH, Ukraine; TGA, Australia; NAFDAC, Nigeria
  - **Regional Harmonisation Initiatives (RHIs):** APEC; ASEAN; EAC; GHC; PANDRH; SADC **Additionally, around 50 regulatory authorities of LMICs are relating to ICH through RHIs.**
  - **International Pharmaceutical Industry Organisation:** APIC
  - **International Organisations regulated or affected by ICH Guideline(s):** Bill and Melinda Gates Foundation; CIOMS; EDQM; IPEC; PIC/S; USP

## Linking PV activities with Regulatory System Strengthening Efforts

### WHO GBT Performance Maturity Levels

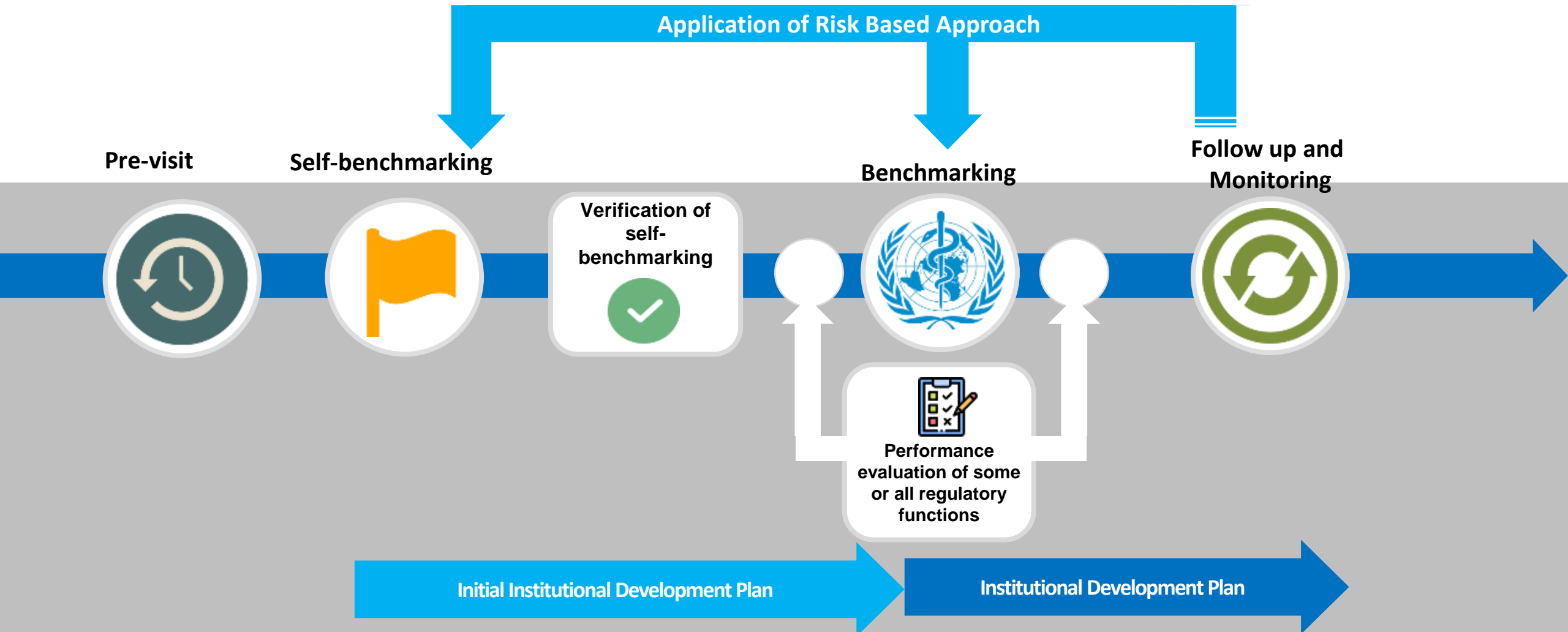


# WHO RECOMMENDED REGULATORY FUNCTIONS FOR MEDICINES AND VACCINES:

## Pharmacovigilance based on product life cycle



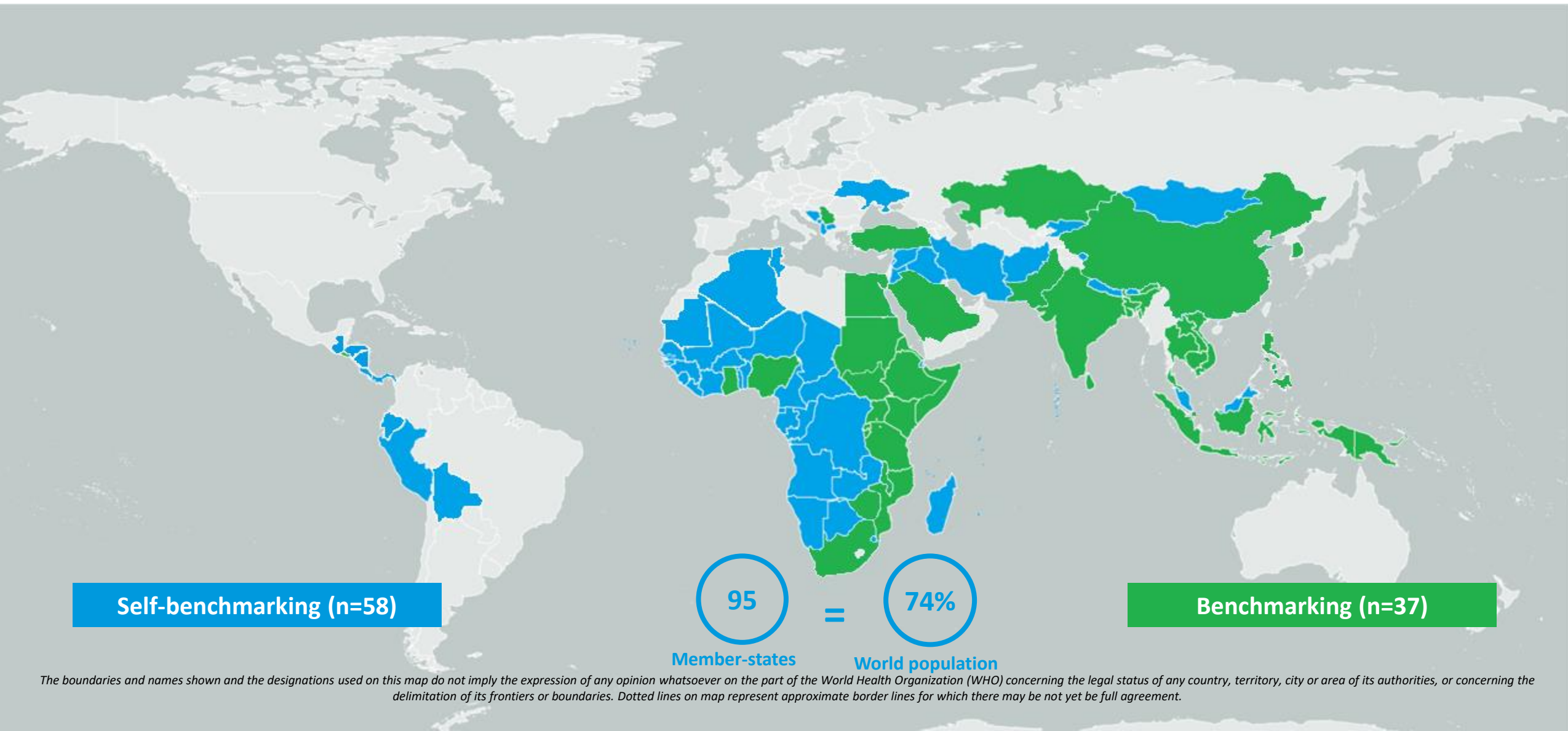
# Benchmarking process



Source: Regulatory System Strengthening (RSS), WHO-HQ

# WHO Regulatory System Strengthening Programme

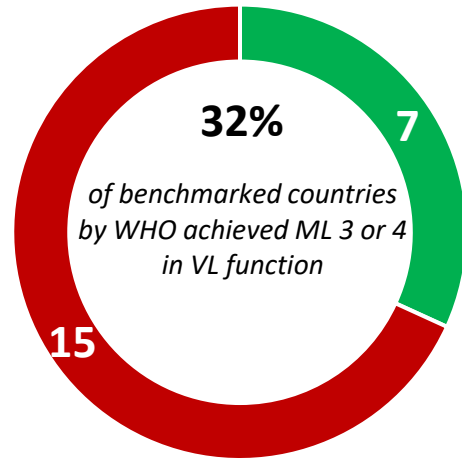
## Global status of benchmarking of regulatory systems (2016 – Nov 2023)



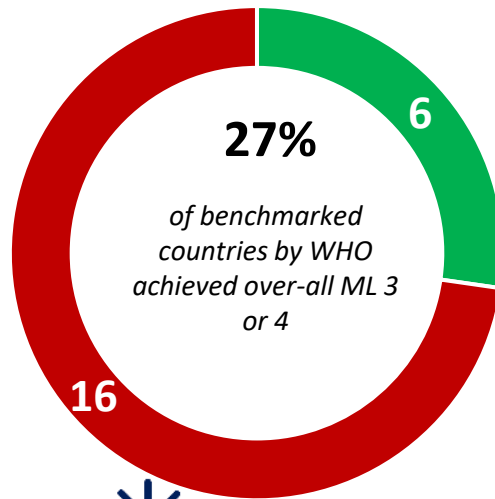
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization (WHO) concerning the legal status of any country, territory, city or area of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on map represent approximate border lines for which there may be not yet be full agreement.

## Status of VL Function and over-all as of the end of 2018

N = 22 benchmarked countries



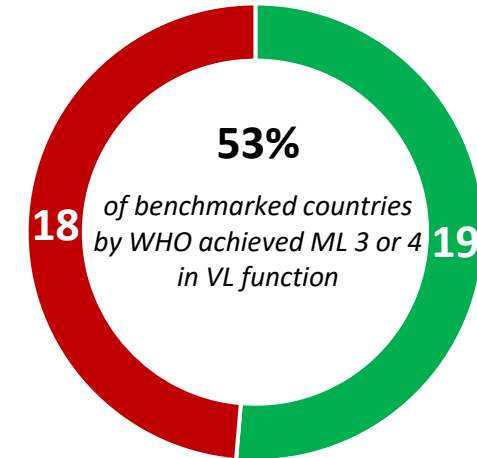
■ VL ML3, ML4 ■ VL ML1, ML2



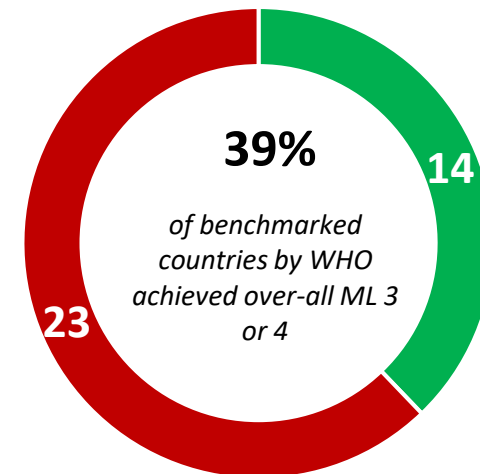
■ Over-all ML3, ML4  
■ Over-all ML1, ML2

## Status of VL Function and over-all as of Nov 2023

N = 37 benchmarked countries



■ VL ML3, ML4 ■ VL ML1, ML2



■ Over-all ML3, ML4  
■ Over-all ML1, ML2

## Number of LMIC countries reporting Serious AEFI to Vigibase 2020 to 2022

Region (LMIC countries 2022)	2020	2021	2022
AFRO (19)	5	16	15
EMRO (7)	6	6	5
EURO (4)	0	4	2
PAHO (4)	1	3	3
SEARO (7)	1	2	1
WPRO (6)	2	4	2
<b>TOTAL (47)</b>	<b>15</b>	<b>35</b>	<b>28</b>

List of LMIC countries from World Bank 2022

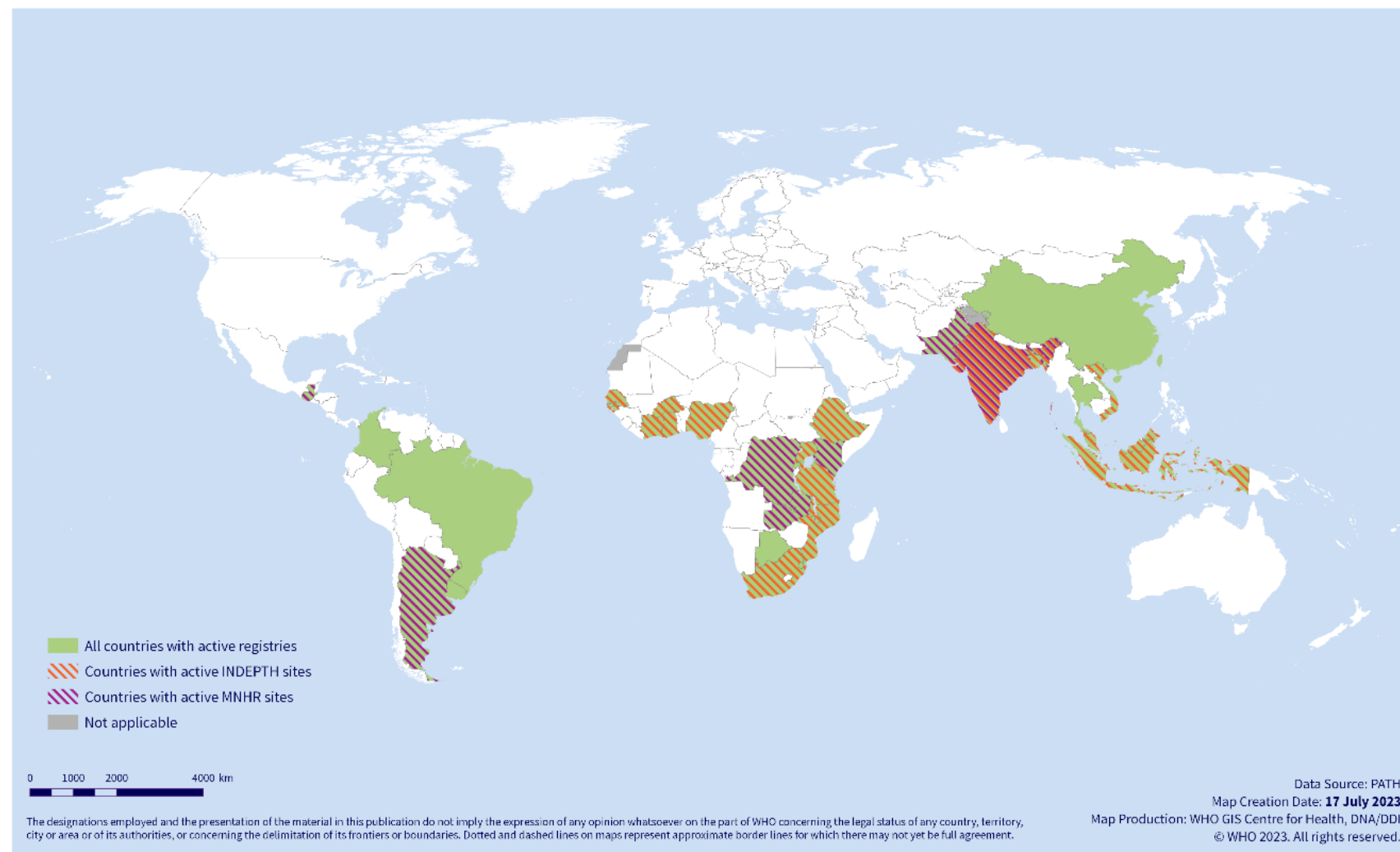
<https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html>

# Pregnancy Exposure Registries in Low- and Middle-Income Countries

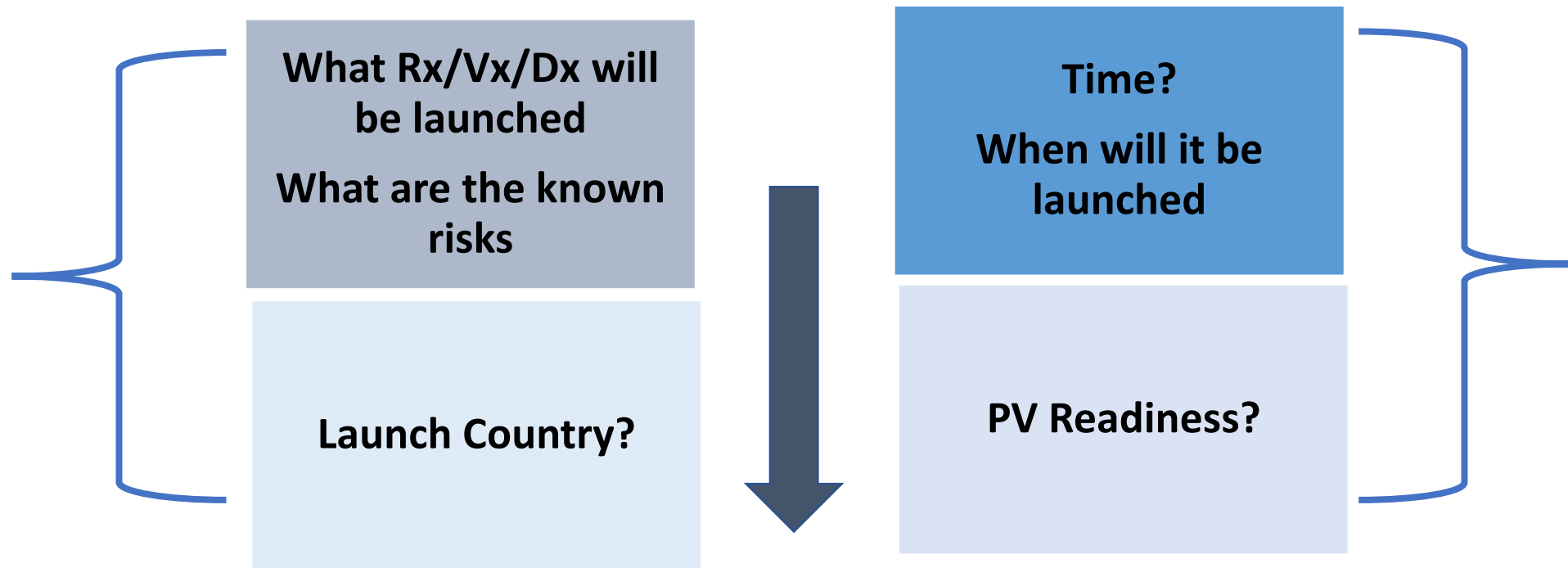
Pregnancy exposure registries and related data collection systems operating in low- and middle-income countries



Resource Category	Number identified (# currently active)
Pregnancy exposure registries	11 (7)
Health and demographic surveillance systems and other observational cohorts	7 (7)
Outcomes-based registries	7 (7)
Maternal condition-based registries	6 (3)
Manufacturer registries	8 (6)
Electronic medical record databases and clinical software platforms	6 (6)
<b>Total</b>	<b>45 (36)</b>



# The Smart PV principles in a nutshell: risk-based prioritization of PV activities



**Assess Regulatory Readiness: Global Benchmarking Tool**  
**Tailor efforts to gaps in the PV systems in targeted countries**



# Smart Safety Surveillance (3S): Multi-Country Experience of Implementing the 3S Concepts and Principles

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**Pilot countries: Armenia, Brazil, Ethiopia, India, Peru, Thailand**



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# Smart Pharmacovigilance Pilot

- Strengthened reporting from public health programmes
- Improved sharing of data
- Enabled Signal detection
- Improved risk management and minimisation
- Strengthened risk communication
- Established the regulatory framework for sustainability



# Thank you

## Is the WHO Smart Pharmacovigilance only for LMIC?



Peter Marks, US FDA, CBER



*'The core principles apply to both low- and middle-income and high-income countries*

*Targeting specific high impact or high-risk products makes eminent sense in terms of resource allocation and return on investment'*

*Pre-ICDRA, Dublin, 2018*