Pharmacovigilance in WHO: new challenges and opportunities

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Objectives

1. Understand the importance of Pharmacovigilance

2. Understand the concept of the WHO Programme for International Drug Monitoring (PIDM)

3. Understand the WHO strategy for Global Pharmacovigilance
Value of medicinal products

- Reduction of morbidity and mortality
- Prolongation of life expectancy
- Eradication of certain diseases
- Improvement of quality of life (QoL)
Drug research and development

Research and Development phase

- **Preclinical**
  - Animal experiments for acute toxicity, metabolism, kinetics etc.

- **Phase I**
  - 20 – 50 healthy volunteers

- **Phase II**
  - 150 – 350 subjects with disease – to determine safety & dosage

- **Phase III**
  - 250 – 4000 more varied patients groups – to determine short-term safety & efficacy

Post MA

- **Phase IV (post-approval)**
- **Spontaneous reporting**

- **Post approval studies to determine specific safety issues**
# Limitations of clinical trials

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<tr>
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<th>Clinical trials (RCT)</th>
<th>Real-world</th>
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<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>Hundreds, rarely thousands</td>
<td>Thousands and millions</td>
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<tr>
<td><strong>Length of study period</strong></td>
<td>Days to months</td>
<td>Days to years</td>
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<tr>
<td><strong>Concomitant treatments</strong></td>
<td>Avoided</td>
<td>Possibly more than one</td>
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<td><strong>Dose</strong></td>
<td>Fixed</td>
<td>Variable in general</td>
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<tr>
<td><strong>Conditions</strong></td>
<td>Rigorous follow-up</td>
<td>Varied follow-up</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Pregnant, children and elderly excluded</td>
<td>Potentially, all the population</td>
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RCT: Randomized Controlled Trial
Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicinal products related problem.
The foundation of the Programme

After the thalidomide disaster

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”.

Thalidomide – children born 1957 - 1963

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

The WHO Programme for International Drug Monitoring (PIDM) is a network that share the vision of safer and more effective use of medicines and vaccines.

They work nationally and collaborate internationally to monitor and identify the harm caused by medicines and vaccines, to reduce the risks to public health and to establish worldwide pharmacovigilance standards and systems.
WHO Programme for International Drug Monitoring (PIDM)

Current membership

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

176 Members in the Programme as of April 2023.
VigiBase

- VigiBase is the unique WHO global database of reported adverse events of medicinal products.
- 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 May 2023, more than 150 Members shared 35,000,000 ICSRs with VigiBase.
Various tools to facilitate Pharmacovigilance work

**VigiFlow** is a web-based pharmacovigilance management system

**VigiLyze** is a signal detection and signal management tool

Images: Uppsala Monitoring Centre (WHO-CC)
VigiMobile

- VigiMobile is a new app developed in technical collaboration with UMC and WHO-GIS.
- Supports electronic **field reporting** of AEFI.
- Based on the **WHO standard reporting form for AEFI**.
- VigiMobile is continuously evolving. **ADR reporting form** is now under integration into VigiMobile.
- Financially sustainable. **Free of charge** for VigiFlow countries 😊

Images: Uppsala Monitoring Centre (WHO-CC)

5/12/2023
Our global network with experts

Two advisory committees

WHO PIDM

WHO Collaborating Centers

Regular exchange with Regulators

Vaccine Safety Net (Communication experts)

WHO PVG

ACSoMP
WHO Advisory Committee on Safety of Medicinal Products

GACVS
WHO Global Advisory Committee on Vaccine Safety

The first ACSoMP/GACVS joint meeting was held in June 2022.
Discussion

1. Who are the stakeholders in pharmacovigilance?
2. How do we support pharmacovigilance activities in a pandemic compared to “normal” times?
3. How do we sustain pharmacovigilance?
From data to decision: the safety process

Safety surveillance of medicinal products

In «normal» times

Adverse Event/Data ➔ Signal ➔ Action

Passive reporting
Active surveillance
Manufacturers

National
Regional
Global

National
Regional
Global

Measures in a pandemic

Daily Intelligence
Reviews

Databases
Networks
Studies
Literature

Triage

Expert
committee

Assessment

Communication
(e.g., public briefings, alerts)

Recommendations for Policies (e.g., SAGE) and product labelling

Watch list
Key learnings from the COVID-19 experiences

Pro-activity

Timely simple data management

More data sources

Collaboration, Coordination
Where do we start: not enough resources to do everything, everywhere, and at once

Prioritize
Apply Smart Principles – value for money
The WHO ‘Smart’ Pharmacovigilance Strategy - Leaning on Learnings

Number of reports on adverse events with medicines

African region | Eastern Mediterranean region | European region | American region | South-East Asian region | Western pacific region

Average # ICSRs submitted to WHO / 100,000 population of reporting countries

2007: Introduction of annual PV Francophone course
2007: Introduction of active surveillance (malaria)
2008: Network of PV consultants for Africa
2010: WHO PV Regional Networks
2012: Patient Reporting
2016: Tools and training

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

Annual meetings hosted in rotation by regions

SOURCE:WHO global database of ICSRs (Vigibase)
Key Themes of WHO’s 13th Draft General Programme of Work 2019-2023

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

Focus global public goods on impact
Mature health system, Fragile health system
Linking PV activities with Regulatory System Strengthening Efforts

WHO GBT Performance Maturity Levels

1. Some elements of regulatory system exist
   - Can be considered functional if rely on other regulators for some specific functions

2. Evolving national regulatory system that partially performs essential regulatory functions

3. Stable, well-functioning and integrated regulatory system
   - Target of WHA Resolution 67.20

4. Regulatory system operating at advanced level of performance and continuous improvement
   - Advanced/reference Regulatory Authorities
Link with GBT Maturity Level (ML) concept – Stepwise Approach to Impact and Sustain

- **Below ML3**
  - Short term: Min PV, Reliance
  - Medium term: Capacity, Competence
  - Long term: Expand Scope

- **At ML3**
  - Short term: In addition, Pilots
  - Medium term: Collaboration, Work-sharing
  - Long term: Expand Scope

- **WLA/Above ML3**
  - Short term: In addition, Technical Support
  - Medium term: Sentinel Sites
  - Long term: Expand Scope
Risk-based prioritization of PV activities

- What Rx/Vx/Dx will be launched
- What are the known risks
- Launch Country?
- Time?
  - When will it be launched
- PV Readiness?

Assess Regulatory Readiness: Global Benchmarking Tool
Tailor efforts to gaps in the PV systems in targeted countries
WHO Strategy for Global Pharmacovigilance

The overall vision, goals and operating principles described in the 3S and GVSB2.0 are mutually relevant for medicines and vaccines safety.
Conclusion

- **Pharmacovigilance** is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicinal products related problem.

- WHO hosts the WHO Programme for International Drug Monitoring and supports countries to strengthen Pharmacovigilance system in collaboration with partners. **Vigi-tools** developed by UMC are an example of technical tools which are offered to the PIDM Members.

- WHO takes the secretariat role to hold the **ACSoMP and GACVS**. Since 2022, these two advisory committees have **jointly discussed issues of common interest** in medicines and vaccines safety.

- In the COVID-19 pandemic, the importance has been highlighted to **have real-time simple data management systems, extend data sources, and to work in collaborative and coordinated manner**.

- The **WHO Global Benchmarking** approach that integrates Vigilance as one of the key regulatory functions within an institutional development plan should provide the relevant framework to sustain the strategies.

- According to the 3S concept, we need to **invest our resources smartly** by focusing on new priority products, sharing work and resources with other countries when possible. The overall vision, goals and operating principles described in the **3S and GVSB2.0** are mutually relevant for medicines and vaccines safety.
PVG Team

- 5 UN regions
- 4 UN languages
Publications – Examples
Policies, guidelines and normative activities

PVG publications can be accessed via:
https://www.who.int/publications/i?healthtopics=c896df17-29f4-4e3a-b811-302f999ed12d_9bc69cb6-e97e-4ae9-adf3-76d9b17f08&publishingoffices=a511529e-adb5-49ea-bbde-546a3c26cba7&healthtopics-hidden=true&publishingoffices-hidden=true&regionscountries-hidden=true
Trainings & other resources

- **Vaccine Safety Basics**
  - https://openwho.org/courses/vaccine-safety-basics

- **AEFI data management eLearning Platform (Harmonia)**
  - http://gvsi-aefi-tools.org/aeidata/training/index1.html

- **AEFI causality assessment software in built-Learning**
  - http://gvsi-aefi-tools.org/

- **ATC-DDD Toolkit**
  - https://www.who.int/tools/atc-ddd-toolkit#:~:text=The%20ATC%2FDDD%20Toolkit%20is,drug%20utilization%20monitoring%20and%20research.

- **PV Toolkit**
  - https://whopvresources.org/

- **UMC e-Learning course**
  - https://learning.who-umc.org/visitor_class_catalog
Thank you