Medicines Safety in WHO: promoting best practices in Pharmacovigilance

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Birth of modern pharmacovigilance

Thalidomide – Phocomelia 1961
Assembly Resolution 16.36 - Clinical and Pharmacological Evaluation of Drugs

INVITES Member States to arrange for a systematic collection of information on serious adverse drug reactions observed during the development of a drug and, in particular, after its release for general use.
Anatomical Therapeutic Chemical (ATC) Classification

Defined Daily Dose (DDD)

- Another WHO Collaborating Centre
  - Drug statistics methodology
- In Oslo, Norway
- International Working Group on Drug Statistics Methodology
- Meets twice a year
- Assigns codes and DDDs
- Integrated into the UMC database
- Need to use better in DUR
Roles and Responsibilities

**WHO**
- Policies and strategies for PV
- Guidelines, norms and standards
- Exchange of information
- Systems strengthening
- Training and capacity building
- Dialogue with donors & public health programmes

**WHO Collaborating Centres**
- Tools and technologies
- Research and Innovation
- Implementation / proof of concept
- Everyday technical support
- Training and capacity building
- Exchange of information
• Technical support
• Network operations
• Implementation
• ADR Database
• Signals
• Capacity building
• Research and development
• Communication
Collaborations & Partnerships within WHO

- Malaria
- HIV/AIDS
- TB
- Neglected tropical diseases
- Patient Safety
- Traditional Medicines
- Vaccines
- Classifications
Advisory Committee on Safety of Medicinal Products (ACSoMP)

The Advisory Committee on Safety of Medicinal Products shall provide advice on pharmacovigilance policy and issues related to the safety and effectiveness of medicinal products:

- to the relevant Assistant Director-General in WHO and through him/her:
  - to the Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre), and
  - to the Member States of WHO.
What defines it
What is pharmacovigilance

• The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems.

(The Importance of Pharmacovigilance, WHO 2002)

• A tool for generating evidence to inform policies
Putting the horse in front of the cart

If there are no systems, there will be no evidence
or any other drug-related problems.

**Diethylene glycol tragedy in Nigeria**

**NAFDAC Nigeria**

- Paracetamol 1989 > 100 deaths (children)

- Paracetamol + Chlorpheniramine 2009 (teething mixture – ‘My Pikin’)
  ~100 deaths (children)
  ~110 Acute renal failure

**PV scope needs to be expanded to address quality issues**
PV definition '... understanding and prevention of adverse effects'

Up to 50% of ADRs are preventable
Pharmacovigilance system that

- Records errors
- Analyses
- Learns
- Implements checks
- Prevents errors

- WHO Guidance document on detecting Medication Errors from PV data
Spontaneous reporting: Bedrock of PV these forty years.

But: Lack of denominator data

Public health programmes need to

- address key safety questions, quickly
- provide rates of AEs
- monitor AEs in special populations (children..)
Addressing the PV needs of public health programmes

- Malaria
- HIV/AIDS

Dystonia with ACTs? Result of malnutrition / repeated treatment with ACTs?

Delete d4t?; NVP in women?
Can we use TDF without renal monitoring?
Risk of severe anaemia in children with AZT?
Use NVP & rifampicin concomitantly in HIV/TB patients?
WHO has developed a protocol for cohort event monitoring (CEM) of:
- antimalarials and
- ARVs

WHO has developed a protocol for Targeted Spontaneous Reporting (TSR):
- TB medicines PV handbook
Understanding what's available and what's needed in countries

Pharmacovigilance Activities in 55 Low- and Middle-Income Countries
A Questionnaire-Based Analysis

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Type of assistance needed

- Technical support / equipment (33)
- Training
- PV in continuing education
- Approaching authorities
- Organizing conferences, networking
- Monitoring & evaluation
- More human resources
- PV in curricula
PV consultants for AFRICA: PVSF

WHO CC for advocacy and training in PV, Accra, Ghana
Technical Solutions for Africa

- **VigiFlow**: tool for national ICSR management and submission to WHO/UMC
  - Provides country with a national database
  - E2b compliant
  - Incorporates MedDRA
  - Free software update and maintenance by UMC

**Challenge**: access to broadband internet

**Solution**: Silverlite
Joint WHO/Global Fund pharmacovigilance strategy

- Establish basic functions and minimum requirements of national pharmacovigilance system
  
- pharmacovigilance toolkit to support training and development
  - Slide 27 (www.pvtoolkit.org)

- Strong wording in Round 10 requesting countries to include PV
Pharmacovigilance Toolkit

Pharmacovigilance Toolkit is a collection of resources and information needed for the practice of pharmacovigilance. The main aim of its development is to ensure that PV practitioners in low- and middle-income countries get access to information on the processes and activities involved in PV from a trusted source. The Toolkit contents are endorsed by the WHO Advisory Committee on the Safety of Medicinal Products after the original text has been written and reviewed by global experts.

In addition to this website, the Toolkit is available on USB drives in a similar format to this website, for use in areas with poor internet connectivity. The Toolkit is currently available in English, and efforts are underway to have it translated into other languages, although this is dependent on availability of volunteers and/or funding. The Toolkit will be reviewed periodically to ensure that it is abreast with developments in PV.

The Toolkit Management Team is keen to have your feedback such as what you think can be added, removed or modified in order to make its use more beneficial.

Development of the PV Toolkit was supported by a generous grant from the Global Fund.

Disease-specific Toolkits

Although this PV Toolkit covers all the basics required for PV work, there are peculiarities when carrying out PV for certain diseases and subgroups of people. This has led to the development of the Malaria and HIV PV Toolkits, with a TB Toolkit currently being developed in addition. These disease-specific toolkits should be used in combination with the main PV Toolkit.

What’s New?

WHO E-learning course on Vaccine Safety

This online course covers main elements of vaccine safety (definitions, introduction of vaccines and AEFI, surveillance, vaccine safety stakeholders and communication). It targets future WHO training participants, NRA and EPI staff in countries, and any other stakeholders working in areas related to vaccine safety.

A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis

Safety Monitoring of Medicinal Products - Reporting system for the general public

Toolkit is managed and maintained by

WHO Collaborating Centre for Advocacy & Training in Pharmacovigilance, University of Ghana Medical School, Accra, Ghana
What gets measured, gets done

- Success indicators
  - Outcomes
  - Impact
“Weber effect” in postmarketing

ADR reports

Dear Healthcare Letter

Drug Approval

Time

Value of patient reports

- Less underreporting
- Patients report different ADRs
- Cover blindspots of pharmacovigilance systems → OTC medication, herbal drugs
- Information about impact on daily life
- Use for signal detection
Background

- If patient reporting is to be recognized as beneficial for pharmacovigilance and further optimized, methodology and best practice must be internationally shared and promoted.
Additional stakeholders: the full picture

- Direct patient reporting
  - WHO guidelines
  - Reporting tool
    - patient organization input
    - Being piloted in Croatia
Our strategy

- Understanding the local needs
- Engaging public health programmes
- Bringing in additional stakeholders
- More patient centred
- Expanding the scope of PV
Thank you

• The impossible: we are on it
• For miracles: expect some delay

Website
www.who.int/medicines/areas/quality_safety/safety_efficacy/en

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