WHO Programme for International Drug Monitoring, Pharmacovigilance Centres & Patient Safety
Birth of WHO Drug Monitoring Programme
Thalidomide – Phocomelia
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.
Pilot project of ten countries

- Australia, Canada, Denmark, Germany, Ireland, Netherlands, New Zealand, Sweden, United Kingdom, USA
WHA23.13 International Monitoring of Adverse Reactions to Drugs

- REQUESTS the Director-General to develop the activities of the project into a primary operational phase aimed at the establishment of an international system for monitoring adverse reactions with provision for alerting Member States in cases of urgency, in accordance with resolution WHA16.36, and to report to the World Health Assembly.
WHO - Swedish Agreement

1978

Agreement signed that the operational activities of the WHO Programme for International Drug Monitoring should be based in Sweden.
WHO Programme for International Drug Monitoring

WHO HQ + 6 Regional offices

National PV Centres

WHO Collaborating Centre, Uppsala
WHO Drug Monitoring Programme
Founding Members 1968
Member countries 1968-2008
Pharmacovigilance in WHO HQ

1. Exchange of Information
2. Policies, guidelines, normative activities
3. Country support
4. Collaborations
5. Resource mobilisation
1. Exchange of Information

- National Information Officers, Regional Offices, Regulators network, Electronic exchange groups (PVSF, Vigimed etc), Annual PV centres meeting

- Publications (WHO Pharm Newsletter, Drug Alerts, WHO Drug Information)

- Conferences and expert committees of Drug Regulatory Authorities (Advisory Committee on Safety of Medicinal Products...)
2. Policies, Guidelines and Normative Activities

- **Guidelines**
  - The Importance of Pharmacovigilance (2002)
  - Policy perspectives on medicines (Pharmacovigilance) 2004
  - Pharmacovigilance in Public Health
  - Advisory Committee for the Safe Use of Medicinal Products (ACSoMP)
3. Country support

- Training courses on pharmacovigilance (Regional Training Courses, biennial course by UMC and HQ)

- Address specific / stated needs: kava, ARVs, antimalarials....

- Annual Meeting of Pharmacovigilance Centres (working groups, break out sessions)

10 courses offered in 2008
Almost 110 million people targeted for either diethylcarbamazine citrate (DEC) plus albendazole or ivermectin plus albendazole

- Malaria
- HIV/AIDS
- Leprosy
- Lymphatic Filariasis
- Patient Safety
- Poisons and Chemicals Safety
- Traditional Medicines
- Vaccines
5. Fundraising

- Gates foundation
- European commission
- Others
WHO Collaborating Centre
the Uppsala Monitoring Centre

- established as a foundation 1978
- based on agreement Sweden – WHO (1978 and revised 2002)
- international administrative board
- WHO Headquarters responsible for policy
- Staff of about 50
Some facts about the UMC

- It is a WHO Collaborating Centre for the WHO PV programme
- Self financing
- 'Products' arm generates revenue
- No profits: foundation
- Where does the money go?

WHO Programme

Funding

Commercial sector activities
Functions

- Receive and manage ADR data
- Develop tools; innovate
- Analyse:
  - Signal detection: Identification of previously unknown drug reactions
- Communicate
- Support countries: train; search; technical assistance
Flow of ADR reports

WHO-ART  ↔  Vigibase  ↔  WHO Drug Dictionary

Own tools  E2B  Intdis  VigiFlow  VigiSearch

National Centre

World Health Organization
Signal Detection & Follow-up

Combinations.db
(reported quarterly)

- 40 experts from around the world
- Select associations for follow-up
- Write signals in the SIGNAL document

Review panel

Yes
No

Follow-up

SIGNAL

Quarterly analysis
BCPNN

Vigibase

Pharma Company

National Centres

World Health Organization
UMC Functions
- a communication centre

- Internet home page
  http://www.who-umc.org

- Vigimed e-mail discussion group

Of interest to safe medication network?
Achievements

- 89 Member countries
- 4 million+ case reports
- Disease driven approach
- Some Public Health programmes 'infiltrated'
- Growing recognition and support

NOT proportionate
At least 2 reasons why we need to re-think our strategy
Reason 1

Preventable harms still occurring

2007
Half of all ADRs are avoidable

ORIGINAL ARTICLE

Adverse drug reactions in hospital in-patients: a pilot study

E. C. Davies*†, MPharm MRPharmS, C. F. Green†, BSc Hons PgDipClinPharm PhD MRPharmS, D. R. Mottram‡, BPharm PhD, FRPharmS and M. Pirmohamed*§, MBchB PhD FRCP

- 125 Patients

- 24 Patients experienced ADRs (19%)

59% of ADRs were avoidable
WHO Programme for International Drug Monitoring started late 60s – early 70s

About 40 years later: less than 100 'full' members

4 million reports

Most reports from developed countries. Why is that?

Why is Pharmacovigilance not getting the attention it deserves
Traditional trends

- Adverse *drug* reaction
- Adverse *drug* event
- *Medicine* safety
- *Medicine* toxicity
- Benefit /harm profile of a medicine
- Product emphatic

Where is the patient?
Need to humanize what we do

- Let's give pharmacovigilance a 'face'
- Let's talk about patient safety, not just medicine safety
- Ask the right question
- Instead of asking 'Is the medicine safe'
- Need to ask:

  *Is the patient safe taking this medicine?*
Am I SAFE with this medicine?

PV is about me !!
Question

Can Pharmacovigilance centres become more patient centred?
Reports of medication errors in WHO ICSR database in 2005

- 2% Medication errors
- 98% Total reports
Reports of medication errors by therapeutic groups in WHO database

- Analgesics: 18.7%
- Antidepressants: 7%
- Antineoplastic agents: 6%
- Antipsychotic agents: 5%
- Antithrombotic agents: 2.4%
Need a system that

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

- Records medication related errors
- Analyses those errors
- Implements interventions
- Promotes patient safety

Actionable learning system
WHO Patient Safety- Pharmacovigilance alliance

- World Alliance for Patient Safety
- To build on medication related expertise of the WHO-PV programme
- Reporting and learning systems
- Collaborative project for the development of pharmacovigilance centres for patient safety
- Partners: WHO-PV, WAPS, UMC, Moroccan centre for poison control and pharmacovigilance
2 Parts: Part 1
At country level

Moroccan centre pilot project:

- A retrospective analysis of spontaneous reports in Moroccan PVC database (2003 – 2006)

- MEs identified (14.4 % of ADEs)

- Some ME characteristics identified
  - stage of ME
  - type of ME

- Medicines involved

- BUT not sufficient information in 'yellow card' for Root Cause Analysis
Part 1 continued

- Moroccan Centre prospective study
- 8 ICU Wards
- 'New' yellow card filled in when ADE identified
- ME form filled-in for each ME detected
625 Patients surveyed
107 INCIDENTS (ADE)

46 Medication Errors

19 Medication Errors with Harm

27 No Harm

61 ADRs

15 Serious
Death: 1
Life threatening morbidity: 5
Hospitalisation/prolonged hospitalisation: 9

33 Serious
Death: 1
Life threatening morbidity: 10
Hospitalisation/delayed hospitalisation: 22
## Root cause analysis

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<th>Objective</th>
<th>Resources</th>
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<td>Description of event (Type, time, consequences....)</td>
<td>Interviewing staff</td>
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<td>Identification of the proximal cause</td>
<td>Interview, case review</td>
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<td>Contributing factors (communication, training, fatigue, equipment)</td>
<td>Interview</td>
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<td>Step 4</td>
<td>Implementing an action plan</td>
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Part 1: conclusions

- Patient safety clearly identified as an existing part of PVC functions

- Develop a plan on how to optimize data capture (for MEs and RCA)
  - Eg what additional elements in reporting form?
  - All reports to have additional info or only those of MEs?
  - Only for some medicines?

- Test 'plan' in additional PV centres

- RCA of optimal information; interventions; measure impact of interventions
Pilot Project: part 2  
(WHO CC as lead investigator)

- Analysed
  - data in WHO ICSR database (Vigibase) for ME

- Pointers for ME
  - Recognition of potential for drug interactions (< 0.5%)
    - are co-reported drugs 'established interactors'?;
    - nature of ARTs (therapeutic level decreased / increased):
  - Drugs most frequently involved in interactions (anticonvulsants, anticoagulants)
  - Prescription of drugs in patients with known contraindications
    - eg beta-blockers in bronchospasm

- Pointers of impact of information
  - Not respecting 'letters'
    - Eg insulin and rosiglitazone concurrent therapy (US FDA warning 2004)
    - 402 reports of the pair in Vigibase, received after warning
Conclusions of Pilot

- Vigibase already contains very useful information to identify and prevent ME.

- Institute an agreed way of identifying more efficiently patient safety reports prospectively.

- Improve terminologies.
  - Additional included terms for broader / better search:
    - 'Medication error': preferred term
    - Accidental overdose, accidental needle stick: included terms

- Longitudinal data sets (prescription records) may be useful complements to spontaneous reporting systems in identifying MEs.

- More effort (education?) needed to communicate patient safety findings.
PV programs may be well-placed to react to medication errors and highlight high-risk medicines.

The current reporting system should be enhanced to capture medication errors.

Guidance for follow up: What should the National Centre do when they receive a report?

Definitions: need to reflect consideration of safety of medication use rather than just medicine safety.

Networking: National Monitoring Centres are unlikely to succeed at this work in the absence of a network.

International Collaboration with data sharing and consequential development of guidance for National Monitoring Centres in relation to medication errors.
Eyes peeled and face forward for patient safety