Requirements for Pharmacovigilance Reporting in SA & New Developments

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OVERVIEW

- Definitions
- Scope of PV
- Aim of PV
- Legal Basis
- PV obligations of the Applicant
- The role of PV Officer
- Procedure for ADR Reporting
- New Developments - PV Tools
- Conclusion
Few Shockers!

- **100 000 deaths** per year in US due to ADRs
  - (4th highest cause of mortality in USA) (Lazarou)
- **3.99 errors per 1,000 medication orders** (IOM report)
- Medication error or adverse effect in **50% of surgical procedures** (Mass Gen Hosp)
- **Approx 6-8%** of all SA hospital admissions are due to adverse reactions (Mehta, Mouton)
  - excluding..overdoses, drug abuse-related reactions and medication errors!
Is PV a bigger problem?

• Thalidomide...need for regulation of medicines (Regulation)
• Ethylene glycol poisonings - product quality problems (GMP)
• Digoxin deaths in France...higher doses used
• St John’s Wort/ kava kava - “natural” ≠ “safe”...phytovigilance
• 1 case of date-rape... unfolds a new culture of drug abuse – “Rohypnol”.
• Meloxicam - fatal GI haemorrhages in France... advertised as safer on the stomach
• Deaths after immunisation... dangerous storage practice
‘vigilance’ in relation to a medicine, medical device or IVD, means the continuous monitoring and evaluation of its safety, efficacy and performance profile and the management of any risk throughout its life-cycle.
Definition of Pharmacovigilance

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

Activities include:
- collection, collation, analysis of ADRs, assessment, detection of signals and
- prevention of adverse reactions to drugs including communication of changes in risk/benefit balance to stakeholders

The Importance of Pharmacovigilance: WHO 2002
Scope of Pharmacovigilance

- reporting of adverse drug reaction/events,
- medication errors,
- interaction of medicines,
- abuse/misuse of medicines,
- overdose,
- Substandard, Spurious, Falsely labelled, Falsified Counterfeits (SSFFCs), and
- lack of effect.
Aim of Pharmacovigilance

- Early detection of unknown adverse reactions and interactions
- Detection of increases in frequency of (known) adverse reactions.
- Identification of risk factors and possible mechanisms underlying adverse reactions
- Estimation of quantitative aspects of benefit/risk analysis and dissemination of information needed to improve drug prescribing
Legal Basis

• Regulation 40 of Medicines and Related Substance Act 101 of 1965

• A person who has applied for registration of a medicines in terms of section 15 of the Act, or a holder of a certificate of registration in respect of a medicine or Scheduled substance, or a holder of a licence in terms of section 22C(1)(b) must inform the Authority, in the manner and within the time frame as determined by the Authority, of any:
Legal Basis cont...

a) New or existing quality, safety or effectiveness concerns related to any medicine or scheduled substance, including but not limited to ADR, and

b) Risk management activities associated with paragraph a).

A health care provider, veterinarian or any other person should inform the Authority, in the manner as determined by the Authority, of any-

(a) suspected adverse drug reactions; or

(b) new or existing safety, quality or effectiveness concerns, occurring as a result of the use of any medicine or scheduled substance.
PV Obligations of the Applicant

- Continuous and routine review of status of all registered medicines
- Appropriate system for PV
- A full-time qualified person(s) responsible for PV
- Timeous submission of ADR reports of all medicines approved by SAHPRA
- Ensure that there is full documentation covering all procedures and activities of PV
The preparation of the following for submission to the Authority:

- adverse drug reaction reports
- SES/Summary report of ADRs (non-serious ADRs)
- Periodic Safety Update Reports (PSURs), when necessary
- company-sponsored post-registration study reports, when required
- ongoing pharmacovigilance evaluation during the post-registration period.
Procedures for ADR Reporting

• **Where to report?**
  – National Adverse Drug Event Monitoring Centre (Cape Town) or
  – Pharmacovigilance Unit (Pretoria)

• **How to report?**
  – Post,
  – Facsimile or
  – Email
  – Use adverse reaction report form or CIOMS
  – E2B/E-Reporting
  – EML Clinical Guide App

• **What to report?**
  – All the relevant information available
  – discharge summaries,
  – post-mortem reports,
  – relevant laboratory data and
  – additional clinical data
The original words/description (verbatim) of the reaction as used by the initial reporter.

The medicine name as reported by the initial reporter, preferably the proprietary name.

Name/initials, email address, telephone number & qualification of the initial reporter.

Additional information, not available at the time of the initial report, should be provided in the form of follow-up reports.
<table>
<thead>
<tr>
<th>Type of ADR Report</th>
<th>Time-frame for reporting</th>
<th>Format</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA Reports (spontaneous/published/study): • Serious (expected and unexpected) • Non-serious (expected and unexpected)</td>
<td>• 15 days • Annually</td>
<td>• ADR form # • SES/Summary report</td>
</tr>
<tr>
<td>Foreign Reports (spontaneous/published/study): Serious</td>
<td>On request or relating to specific safety issue</td>
<td>As appropriate</td>
</tr>
<tr>
<td>Type of ADR Report</td>
<td>Time-frame for reporting</td>
<td>Format</td>
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<tr>
<td>----------------------------------------------------------------------------------</td>
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<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Notification of Change in Nature, Severity or Frequency or Risk factors</td>
<td>3 days</td>
<td>Detailed report (including publications)</td>
</tr>
<tr>
<td>New information impacting on benefit-risk profile of medicine including decisions by national medicines regulatory authorities other than SAHPRA</td>
<td>3 days</td>
<td>Detailed report (including publications)</td>
</tr>
</tbody>
</table>
PV Tools - VigiFlow

- Web-based Individual Case Safety Report (ICSR) management system
- Supports collection, processing and sharing of data of ICSRs
- Facilitate effective data analysis
- Maintained by Uppsala Monitoring Centre (UMC).
- Different access rights and password control
Facilitates quality of data entry
- Error checks and lexicons
- Mandatory fields
- Help texts

Integrated terminologies facilitates drug and ADR coding

Easy communication between regional and national centres

Available in four different languages
PV Tools - VigiFlow

• Features
  ▪ Manual data entry
  ▪ Supports ICSR data sharing & exchange (import & export)
  ▪ Compatible with the ICH-E2B standard for electronic transmission of ICSRs.

• VigiFlow - Used for:
  – Data entry
  – Assessment
  – Storage
  – Retrieval (e.g. follow-ups)
  – Admin statistics
  – Data exchange – Electronic ICSR import & export
• **E2B**
  - standard for sharing drug safety information
  - developed by ICH
  - primarily used for reporting of suspected ADRs in the Post Marketing phase and Clinical Trials.
  - defines the transmission of individual ADR reports bundled in batches. i.e. it is not a standard for transfer of summary data.
Only correct E2B files in xml format can be imported
Generate report Id during import
Upload & process
Generate acknowledgment files
E-Reporting

Confirmation email

Reporters → eReporting → VigiFlow National ICSR Database → VigiBase WHO global ICSR database
• Newly released module for Vigiflow data management system which allows capturing of ICSRs directly from the source into the Vigiflow database

-achieved by creating an open link on the regulator’s website.

-open link transfers data automatically to Vigiflow database.

-Only minor manual data entry

- No delay in receiving the reports

-Available to NCs using VigiFlow complete access
Future PV Plan

VigiFlow can be simple or advanced depending on the needs of the country.
VigiBase

- WHO global database of ICSRs
- Over 16 million reports of suspected adverse effects of medicines
- Linked to medical & drug classifications e.g. WHO-ART, MedDRA, WHO ICD & WHODrug
- Ensures early identification of signals
VigiLyze

- All 15 million ICSRs
- Search parameters
  - Quick Search
  - Specific filters
  - Drill down in chart

- ICSRs of interest
- Statistics view
  - Screen shot
  - PDF export
- ICSR view
  - Excel export

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NDP
Conclusion

Poor quality data → risk of drawing wrong or delayed conclusions about a single case report or a safety signal → could lead to patients being harmed unnecessarily