The National Vigilance policy for Health Technologies

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National Vigilance Policy

- Policy – A principle, plan, or course of action, as pursued by a government, organization, individual, etc.
- Please refer to any associated documents
  - Act 101 as amended,
  - Medicines and related Substances Act 101-1965 - Regulations relating to Medical Devices
  - Recalls_Vigilance_Medical_Devices_IVDs_Nov19_v3

Introduction

- Medical device manufacturer's regulatory obligations continue throughout the device's lifecycle and long after the sale to a customer
- Vigilance vs Manufacturers postmarket surveillance duties
  - Processes are interrelated but should be distinguished
  - Postmarket surveillance is a process for understanding experience (NB risk management element) with the device through systematic feedback and review > ISO13485 Sec 8.2.1
  - **Post market surveillance** – reduce the likelihood of the same adverse incident being repeated in different places at different times
  - **Vigilance** is the reactive element – acting on reports, communicating with CA on these reports, initiating FCA etc.
- Post market surveillance in Acts, laws ,directives and regs and standards… ISO13485 and ISO14971,
  - ISO13485 Sec 8.2.1 states the manufacturer "shall establish a documented procedure for a feedback system to provide early warning of quality problems and for input to the corrective and preventive action process"
  - "if national or regional regulations require the organization to gain experience from the postproduction phase, the review of this experience shall form part of the feedback system"

Purpose

- The primary purpose of this document is to provide guidance to healthcare providers and patients in the post-marketing surveillance of medicines and other health technologies, both in the private and public sectors, thereby contributing to the regulatory objective of ensuring that health products used in clinical practice and domestic settings are safe, effective and of acceptable quality and performance.
- The document gives an overview of what health technology vigilance is, how to detect and classify adverse drug reactions (ADRs) and the structural organization of the vigilance system in SA. It also describes the reporting procedures and protocols to SAHPRA, as mandated by the Medicines and Related Substances Act 101 of 1965 (as amended) to oversee the safety, efficacy, quality and performance of health products in SA and the expected post-reporting outcomes.
- The document also encourages all healthcare providers and patients to participate in vigilance-related activities and to report all suspected ADRs and other health technology-related events to help safeguard the health of all South Africans.

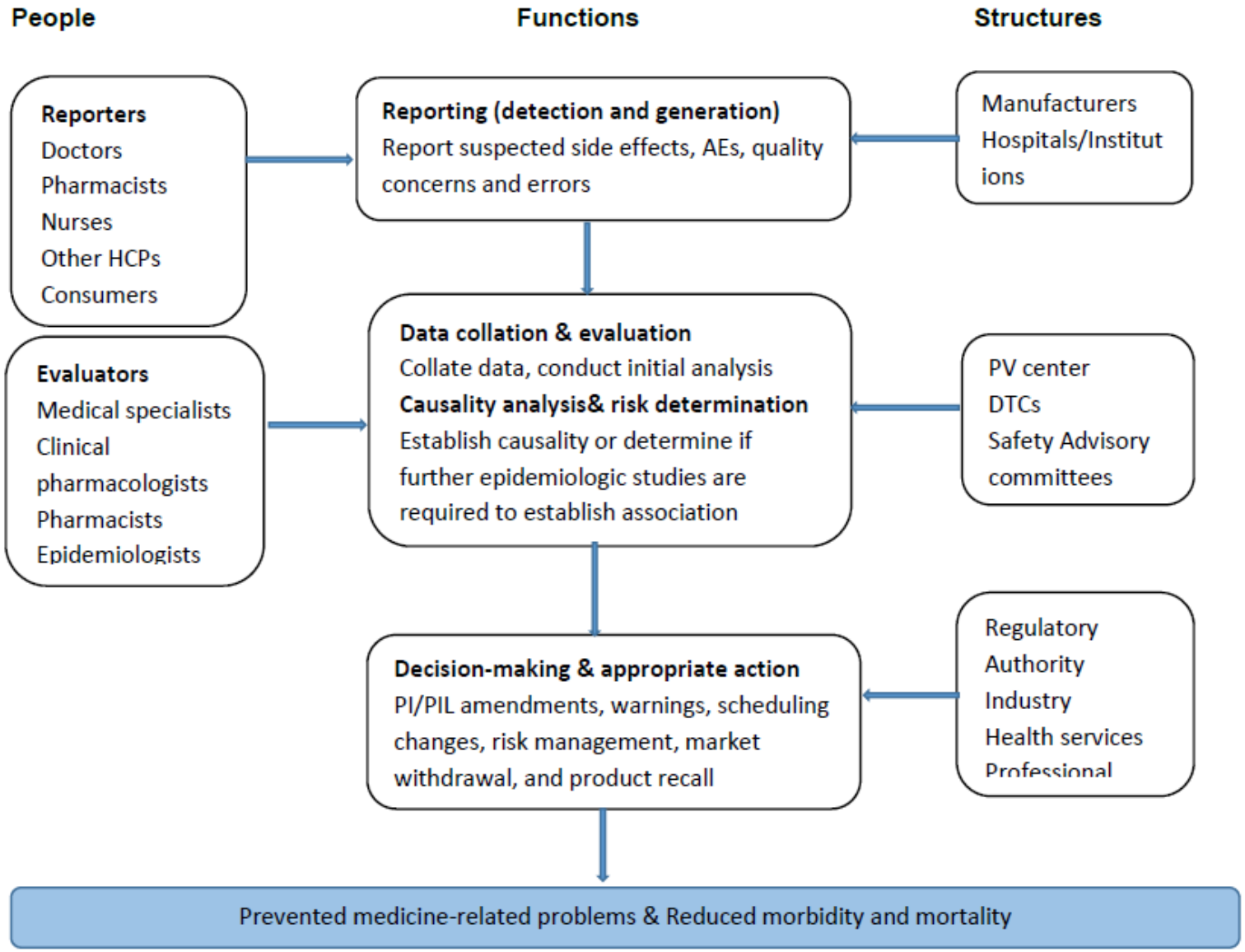
Legal Framework

- SAHPRA was established following the promulgation of the Medicines and Related Substance Amendment Act No. 72 of 2008 and Act 14 of 2015. SAHPRA replaced the Medicines Control Council (MCC), and has the broad legislative mandate of monitoring, evaluation, regulation, investigation, inspection, registration and control of medicines, scheduled substances, clinical trials, medical devices and related matters in the public interest.
- In order to achieve its objectives the Authority must, among other and equally important objectives:
  - Ensure that evidence of existing and new adverse events and reactions, interactions, and signals emerging from post-marketing surveillance and vigilance activities are investigated, monitored, analyzed and acted upon through an effective vigilance system.
- In relation to a medicine, medical device or IVD, '**Vigilance**' means the continuous monitoring and evaluation of its safety, efficacy and performance profile and the management of any risk throughout its life-cycle.

Legal Framework cont'd…

- According to *Regulation 40* of the Medicines and Related Substances Act 101 of 1965, as amended:
- (1) A person who has applied for registration of a medicine in terms of section 15 of the Act, 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 –
  - new or existing quality, safety or effectiveness concerns related to any medicine or scheduled substance, including but not limited to adverse drug reactions; and
  - risk management activities associated with paragraph (a).
- (2) A person who has applied for registration of a medicine in terms of section 15 of the Act, 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 maintain or have access to records of the reports and case reports referred to in subregulation (1) above.

South African Pharmacovigilance Framework



Functions of the Vigilance Unit and vigilance systems

- Functions
- Reporting Tools
  - ADR Reporting form
  - CIOMS (council for International Organisations of Medical Sciences) reporting forms
  - EML Clinical Guide
  - Vigiflow
  - eReporting – module for vigiflow
- Harmonizing medicines safety practices
  - E2B – int std for transmitting medicine AE
  - WHODrug - international reference for medicinal product information
  - MedDRA Specific and standardised medical terminology dictionary – incl drug device combination products

Functions of the Vigilance Unit and vigilance systems cont'd…

- VIGILANCE AWARENESS, TRAINING AND CAPACITY BUILDING
  - South African healthcare providers and consumers need to be trained on vigilance and the reporting system in the country.
  - Priority needs to be given to healthcare providers since this is in-line with their professional responsibilities to ensure rational drug use and appropriate pharmaceutical care.
  - ADR identification and reporting are not well understood and are seldom reported, therefore signals are hardly detected in the country
- In the initial stage, the training is planned as:
  - A rapid cascade followed by a continuous training (with other training programs) to reach out to all pharmacists, clinicians and nurses.
  - SAHPRA will achieve this in collaboration with other various programs such as:
    - Programmatic Pharmacovigilance Directorate of the National Department of Health, where SAHPRA training initiatives will be integrated with on-going training in the sector
    - Internship service training programmes of all healthcare providers, by inclusion of vigilance training.
    - Undergraduate pharmacy and medical curricula, by inclusion of vigilance training.
    - Office of Health Standards Compliance (OHSC), by including vigilance infrastructure in facility assessment tools for both clinics and hospitals of all levels.

METHODS USED TO COLLECT SAFETY INFORMATION IN VIGILANCE

- Spontaneous Reporting - **voluntarily** reported to either the pharmaceutical manufacturers, or provincial pharmacovigilance centers, or to national regulatory authorities by healthcare professionals, patients or consumers, also known as passive reporting. Most common method of surveillance
- individual case safety reports (ICSRs) will take over from Spontaneous reporting – more used for generating hypothoses than verifying association.
- Stimulated reporting
- Targeted Spontaneous reporting
- Active (Proactive) Surveillance – followup after treatment
- Cohort event monitoring
- Prescription even monitoring
- Sentinel Sites
- Registeries
- Observational Studies
- etc., etc.

Data Management Medication Errors

- DATA ANALYSIS & MANAGEMENT OF INDIVIDUAL CASE SAFETY REPORTS (ICSRS), CAUSALITY ASSESSMENT AND SIGNAL DETECTION

- MEDICATION ERRORS AND THE ROLE OF THE PHARMACIST

Reporting of ADR

- Who; What; Which; When; Why

- SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS (SF), AND PRODUCT DEFECTS
  - Product defects
  - https://www.sahpra.org.za/wpcontent/uploads/2020/01/Recalls_Vigilance_Medical_Devices_IVDs_Nov19_v3.pdf

What happens to reports

- Received reports are screened and checked for validity, duplication and eligibility.
- A valid report must contain four minimum data elements, which are suspect drug, ADR, patient and a reporter.
- In order to check for duplicate reports, certain characteristics of an ADR report may be used to identify duplicate reporting or follow up reports, for example, patient name, sex, date of birth or age, suspected drug name, dates of drug exposure, source of reported information (e.g. same journal and different sender) etc.
- Reports are then captured into the individual case safety report management system, called VigiFlow® by senior admin officers
- Each report is allocated a unique report ID number by the system, which is written on each report.
- Quality verification of the captured information follows. This is conducted by technical officers, who are pharmacists by profession.
- Reports are then assessed for causality before submitting to the UMC VigiBase®
- All adverse events are risk assessed and entered into the appropriate database for future reference. The information is used by SAHPRA to help identify safety signals. A safety signal is a 'flag' for a possible safety concern. When SAHPRA identifies a signal, it undertakes a detailed evaluation to establish the possible role of the health product in causing the adverse event.

Feedback to reporters

- The pharmacovigilance unit of the Authority provide an acknowledgment letter as a form of feedback to anyone who reports an ADR and provide contact details of the reporter
- Furthermore, feedback is also provided in a form of DHCP letter, press releases, medicine safety alerts and news bulletin
- Individualized feedback is also provided in specific cases

Guidelines for reporting ADR - MAH

Developing a Pharmacovigilance plan

- For most products, routine pharmacovigilance (i.e., compliance with applicable post market requirements) is sufficient for post-marketing risk assessment. However, in certain limited instances, unusual safety risks may become evident before approval or after a product is marketed that could suggest that consideration by the applicant/MAH of a pharmacovigilance plan may be appropriate. A pharmacovigilance plan is a plan developed by the applicant/MAH that is focused on detecting new safety risks and/or evaluating already identified safety risks.
- decision to develop a pharmacovigilance plan be based on scientific and logistical factors, including but not limited to the following:
  - The likelihood that the adverse event represents a potential safety risk;
  - The frequency with which the event occurs (e.g., incidence rate, reporting rate, or other measures available);
  - The severity of the event;
  - The nature of the population(s) at risk;
  - The range of patients for which the product is indicated (broad range or selected populations only); and
  - The method by which the product is dispensed (through pharmacies or performance linked systems only).

Conclusion

- A Post market surveillance system is important for better health and safety protection of patients, users and others
- Manufacturers are required to implement a PMS system to monitor post production performance in a proactive and systematic manner according to the applicable medical device laws and regs.
- **Vigilance Reporting**; reporting vigilance events; conducting FCA; maintaining PMS; abiding by laws and regulations
- Update QMS; perform internal audits and ensure device safety and performance levels are maintained
- Whilst the policy is seemingly directed at Pharma, there is still a requirement for Medical Device Industry
- *Postmarket lifecycle management may be the most resource-intensive phase for MD manufacturers*