SAHPRA
South African Health Products Regulatory Authority

# THE HEALTH PRODUCTS VIGILANCE FRAMEWORK

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# DOCUMENT REVIEW AND APPROVAL

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## Distribution List

| UNIT/ ENTITY | DESIGNATION |
|---|---|
| SAHPRA | National Pharmacovigilance Steering Committee |
| Clinical Evaluations Management | Manager |

# Contents

## 1. PURPOSE

1.1. The National Health Product Vigilance Framework is designed as a living document that describes the current health product vigilance system and the integrated vigilance system approach that SAHPRA has embarked on to improve regulatory efficiency and harmonisation. The framework also outlines the key stakeholders including their responsibilities and strategies to optimise the vigilance system and harmonise vigilance activities in South Africa.

1.2. This framework further serves as a road map to achieve a more advanced national vigilance system that:

- adopts a harmonised and integrated approach to vigilance within the country
- strengthens vigilance practices, awareness and knowledge
- fosters effective collaboration and engagement with vigilance stakeholders with clearly defined roles and responsibilities
- provides clarity and transparency on vigilance information, processes and decisions , and
- aligns vigilance activities with international best practices.



## 2. SCOPE

2.1 The National Health Product Vigilance Framework considers all vigilance activities for registered health products, which include but are not limited to data collection, monitoring, processing, evaluation, risk communication and market interventions that support and enhance safety surveillance throughout a product's life cycle during the post-marketing phase. The framework considers health products registered for human use including medicines, biological products, complementary medicines, medical devices and in vitro diagnostics (IVDs).

2.2 This framework does not cover the vigilance activities concerned with the product at the pre-marketing phase.

## 3. DEFINITIONS

3.1. The following terms are used in this document:

| Abbreviations/ Terms | Meaning |
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| Active surveillance | The collection of safety information as a continuous pre-organised process. Active surveillance can be medicine-based (identifying adverse effects in patients taking certain medicines), setting-based (identifying adverse effects in certain healthcare settings where patients are likely to present for treatment) or event-based (identifying adverse effects that are likely to be associated with medicines). |
| ADR (Adverse Drug Reaction) | A response to a medicine which is noxious and unintended, which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. |
| AEFI (Adverse event following immunisation) | Any untoward medical occurrence which follows immunisation, and which does not necessarily have a causal relationship with the usage of the vaccine. The AE may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease. |
| AE (Adverse event) | Any untoward medical occurrence that may present during treatment with a health product, but which does not necessarily have a causal relationship with this treatment. |
| Adverse effect | A negative or harmful patient outcome that seems to be associated with treatment, including there being no effect at all. |
| Benefits | Are the positive therapeutic effects or outcomes of treatment in an individual. Benefits also refer to the positive health, social or psychological effects of treatment from the patient's perspective. |
| Benefit-Risk Assessment | An evaluation of the positive therapeutic effects of the medicine in relation to its negative effects (any risk relating to the quality, safety or efficacy of the medicine in regard to patients' health or public health). |
| Causality Assessment | The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. |
| Causal relationship | The likelihood that a medicine is the cause of an observed AE, which can range from certain to unlikely. |
| Clinical Trial | A research study, in a defined and controlled setting, where participants are assigned prospectively to one or more (or no) interventions to evaluate the effects of the intervention on biomedical or health-related outcomes. |
| Clinical Trial Sponsor | Refers to an individual, company or organisation that takes responsibility for initiating, managing and or financing a clinical trial. The sponsor is accountable for overall quality and integrity of the trial. |

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| Consumer | A consumer in relation to healthcare, means a person who uses or is a potential user of health services, as well as their family and caregivers. |
| Counterfeit Medicine | Counterfeit medicine means a medicine in respect of which a false representation has been made about its contents, identity or source by any means including its labelling and packaging. |
| CIOMS (Council for International Organisations of Medical Sciences) | CIOMS is an international, non-governmental, non-profit organisation established jointly by WHO and UNESCO in 1949. CIOMS represents a substantial proportion of the biomedical scientific community through its member organisations, which include many of the biomedical disciplines, national academies of sciences and medical research councils. |
| eCTD (Electronic Common Technical Document) | A standard electronic format for submitting regulatory information such as applications dossiers, supplements and reports) to regulatory authorities. |
| EURD (European Union Reference Date) | Refers to the date of first (or earliest known) marketing authorisation in the European Union (EU) for a medicine containing a specific active substance or combination of substances. This date is used for determining the frequency of periodic safety update reports (PSURs) and related data lock points. |
| HCP (Healthcare professional) | A person providing health services in terms of any law, including in terms of the:<br>(a) Allied Health Professions Act, 1982 (Act No. 63 of 1982),<br>(b) Health Professions Act, 1974 (Act No. 56 of 1974),<br>(c) Nursing Act, 1978 (Act No. 50 of 1978),<br>(d) Pharmacy Act, 1974 (Act No. 53 of 1974),<br>(e) Dental Technicians Act, 1979 (Act No. 19 of 1979). |
| Health Product | Any health-related product including in vitro diagnostics, medical devices, medicines, vaccines and veterinary medicines used in the provision of health services and as defined in Section 1 of the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965) as amended. |
| HIV (Human Immunodeficiency Virus) | HIV is a virus that attacks the body's immune system, specifically the CD4 cells (T cells), making individuals more vulnerable to infections and diseases. |
| Holder of a Certificate of Registration (or applicant) | A person in whose name a registration certificate has been granted and who is responsible for all aspects of the medicine, including quality and safety and compliance with conditions of registration. |
| ICSR (Individual case safety report) | A report that contains information describing a suspected ADR related to the administration of one or more medicinal products to an individual patient. |

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| IVD (In vitro diagnostic) | A medical device, whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. |
| Knowledge Hub | An online training platform for HCPs and the public which connects trainees to relevant, up-to-date professional development opportunities and resources. The Knowledge Hub provides relevant continuous professional development opportunities and up-to-date information and policies on rational use of medicines. |
| Medical Device | Medical device means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, including Group III and IV Hazardous Substances contemplated in the Hazardous Substances Act, 1973 (Act 15 of 1973) intended by the manufacturer to be used, alone or in combination, for humans or animals, for one or more of the following:<br>• diagnosis, prevention, monitoring, treatment or alleviation of disease;<br>• diagnosis, monitoring, treatment, alleviation of or compensation for an injury;<br>• investigation, replacement, modification or support of the anatomy or of a physiological process;<br>• supporting or sustaining life;<br>• control of conception;<br>• disinfection of medical devices; or<br>• providing information for medical or diagnostic purposes by means of in vitro examination of specimens derived from the human body; and<br>• •which does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on human or animal body, but which may be assisted in its intended function by such means. |
| MedDRA (Medical Dictionary for Regulatory Activities) | Medical terminology developed by the ICH with an emphasis on ease of use for data entry, retrieval, analysis and display. |
| Medication Error | Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the HCP, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems including:<br>• prescribing errors; |

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| | • dispensing errors;<br>• medicine preparation errors;<br>• administration errors and<br>• monitoring errors.<br>Medication errors and medicines-related AEs have important implications – from increased length of hospitalisation and costs to undue discomfort and disability or increased mortality. Thus, minimizing of medication errors, through early detection and clinical audit, is of paramount importance in healthcare by promoting compliance, adherence, recovery and the general well-being of patients. |
| Med Safety App | A free smart phone app for reporting of suspected ADRs/AEFIs to Regulatory Authorities, developed by the United Kingdom (UK)'s Medicines and Healthcare Products Regulatory Agency (MHRA) as part of the Innovative Medicines Initiative WEB-Recognising Adverse Drug Reactions (WEB-RADR) project. |
| Medicine | Any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in—<br>i The diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state or the symptoms thereof in humans; or<br>ii Restoring, correcting or modifying any somatic or psychic or organic function in humans; and includes any veterinary medicine. |
| NdoH (National Department of Health) | NDoH is the department in South Africa responsible for providing a framework for a structured and uniform health system in the country. It derives its mandate from the National Health Act of 2003, which outlines the responsibilities of three levels of government in delivering health services. |
| NPC (National Pharmacovigilance Centre) | A single, governmentally recognised centre (or integrated system) within a country with clinical and scientific expertise to collect, collate, analyse and give advice on all information related to medicine safety. |
| NPVSC (National Pharmacovigilance Steering Committee) | The purpose of the NPvSC is to strengthen coordination and collaboration between SAHPRA, national and provincial health authorities to standardise pharmacovigilance structures, systems and ADR reporting tools in South Africa and to improve pharmacovigilance awareness and education among HCPs through training and capacity building initiatives. |

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| NRA (National Regulatory Agency) | An agency responsible for ensuring that health products released for public distribution in a country are evaluated properly and meet international standards of quality and safety and efficacy. |
| Passive surveillance | Passive surveillance involves collecting, analysing, and interpreting unsolicited reports of suspected AEs. It relies on spontaneous reporting, where HCPs and patients voluntarily report suspected AEs to pharmaceutical companies, regulatory authorities, or other relevant organisations. |
| PBRER (Periodic benefit risk evaluation report) | A safety report on evaluation pertaining to the benefit/risk balance of a medicine that is prepared by the HCR. A PBRER is focused on summary information, scientific safety evaluation and integrated benefit/risk evaluation. PBRERs are extremely important in terms of providing information on whether or not there are new risks, the risks have changed or there has occurred a change in the medicine's benefit/risk ratio and are in this regard related to the risk management plan. |
| PSUR (Periodic safety update report) | A periodic report produced by an HCR intended to provide an update of a worldwide safety experience of a medicinal product to regulatory authorities at defined times post marketing authorisation. PSURs include systematically detailed lists of individual cases or case descriptions. |
| PV (Pharmacovigilance) | The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problem. |
| PHP (Public Health Programme) | PHP are organised efforts aimed at protecting and improving the health of communities through disease prevention, health promotion and education. |
| PMS (Post-Marketing Surveillance) | The practice of monitoring safety and effectiveness of health products after registration and released on the market with the objectives to decrease mortality and morbidity associated with AEs and improving understanding of effectiveness in real-world situations. |
| Product quality problem | Product quality problems include concerns about the quality, authenticity, performance, or safety of any medicine medical device or IVD. Problems with product quality may occur during manufacturing, distribution, or storage and include a suspect counterfeit product; product contamination; defective components; poor packaging or product mix-up; questionable stability; medical device malfunctions and labelling concerns. |

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| PI (Professional information)/ PIL (Patient information leaflet) | The product information for a specific health product as approved by NRAs serves as the basis of information for HCPs (PI) or patients (PIL) respectively on how to use the product safely and effectively. A PI is also known as the summary of product characteristics. |
| QPPV (Qualified Person for Pharmacovigilance) | A Qualified Person Responsible For Pharmacovigilance (QPPV) is an individual, on full-time employment by the HCR, who is responsible for overall pharmacovigilance for all medicines of the HCR. The QPPV is responsible for ensuring that the company (the HCR) meets its legal obligations for monitoring of the safety of the products marketed in South Africa, including the establishment and maintenance of the HCR's pharmacovigilance system, preparation pharmacovigilance reports, acts as a single contact point for the regulatory authority on a 24-hour basis and respond to any regulatory queries. |
| RRA (Recognised Regulatory Authority) | An RRA refers to a refers to a national or regional regulatory body that has the legal mandate and technical capacity to oversee the regulation of health products across their life cycle. These bodies meet high standards of oversight and their decisions, assessments, or approvals on health product safety, efficacy, and quality are considered reliable and may be relied upon or referenced by other countries or international bodies. |
| Reporter | Any person, patient or HCP or institute who submits safety information on a suspected adverse effect associated with a specific health product to the National Pharmacovigilance Centre or any other relevant organisation. |
| Risk | The probability (chance, odds) of harm (negative) being caused/occurring. The risks of medicines are possible unwanted or unexpected events (harm) that might happen to the consumer/patient during the use of that medicine. |
| Risk Management Plan | A detailed description of the risk management system. A plan that identifies or characterises the safety profile of the health product(s) concerned, indicates how to characterise further the safety profile of the health product(s) concerned, documents measures to prevent or minimise the risks associated with the health product, including an assessment of the effectiveness of those interventions and document post-authorisation obligations that have been imposed as a condition of the marketing authorisation. |
| Serious adverse event or adverse drug reaction | Any untoward medical occurrence that results in death, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity or is life-threatening. |

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| Side effect | Any unintended effect of a health product occurring at normal dosage which is related to the pharmacological properties of the medicine |
| Signal | Reported information on a possible causal relationship between an AE and a health product, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending on the seriousness of the event and the quality of the information. |
| Signal detection | The act of looking for and/or identifying signals using event data from any source. |
| SAHPRA (South African Health Products Regulatory Authority) | The NRA for South Africa tasked with regulating (monitoring, evaluating, investigating, inspecting, and registering) all health products. |
| Spontaneous ADR reporting | An unsolicited communication of suspected ADRs by an HCP or consumer to a company or regulatory agency which fulfils the following three conditions:<br>a) It describes one or more suspected ADRs in a patient.<br>b) The patient was given one or more medicines.<br>c) It does not derive from a study or organised data collection scheme.<br>Spontaneous reporting is the most common form of passive surveillance. |
| Summary of medicine safety regulatory decisions | A document published by SAHPRA which provides an overview of the safety regulatory decisions taken by the Authority. This includes a summary of regulatory decisions where safety concerns were reviewed and concluded, and those safety concerns that are not concluded but are severe and serious in nature. |
| Unexpected adverse drug reactions | The nature, specificity, severity, and outcome of the adverse reaction are not consistent with the term or description in the local product information or expected from the medicine's known characteristics. When an HCR is uncertain whether an ADR is expected or unexpected, the ADR should be treated as unexpected. An expected ADR with a fatal outcome should be considered unexpected unless the local/regional product information states explicitly that the ADR might be associated with a fatal outcome. |
| UMC (Uppsala Monitoring Centre) | The UMC is the WHO Collaborating Centre for International Drug Monitoring and has been responsible for the technical and operational aspects of the Programme for International Drug Monitoring (PIDM) since 1978. The UMC works by collecting, assessing and communicating information from member countries' national pharmacovigilance centres concerning the benefits, harm, |

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| | effectiveness and risks of medicines. The UMC is responsible for:<br>• Co-ordination of the WHO PIDM and its member countries.<br>• Collection, assessment and communication of information from member countries about the benefits, harms and risks of medicines and other substances.<br>• used in medicines to improve patient therapy and public health worldwide.<br>• Collaborating with member countries in the development and practice of the science of pharmacovigilance. |
| VigiAccess® | A web application that allows the public to access VigiBase® and retrieve statistical data on the suspected ADRs/AEFI of medicines/vaccines reported to the WHO PIDM. |
| VigiBase® | The WHO global database of ICSRs. It is developed and maintained by the Uppsala Monitoring Centre (UMC) on behalf of WHO and its member countries. It consists of reports of ADRs/AEFIs to medicines/vaccines received from member countries since 1968. It is updated with incoming case reports on a continuous basis. The purpose is to ensure that early signs of previously unknown medicines-related safety problems are identified as rapidly as possible. Contrary to VigiAccess®, consumers and HCPs do not have access to VigiBase® database. |
| VigiFlow® | A web based ICSR management system. VigiFlow® supports the collection, processing and sharing of data of ICSRs to facilitate effective data analysis. |
| VigiMobile® | A customisable web application for reporting AEs for medicines and vaccines, available as a free add-on to VigiFlow®. VigiMobile® can be installed on any device and any operating system, making it easily accessible to both patients and HCPs. |
| Vigilance | 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. |
| Vigilance Hub | Refers to the back-end system that supports the Med Safety App. |
| Vigilance unit | Refers to the Pharmacovigilance unit at SAHPRA. |
| World Health Organisation Programme for International Drug Monitoring | The PIDM was established in 1968, to ensure that evidence about harm to patients was collected from as many sources as possible. This would enable individual countries to be alerted to patterns of harm that were emerging across the world, and which might not be evident from their local data alone. The PIDM consists of a group of more than 180 member countries (South Africa became a full member in 1992) that share the vision of safer and more effective use of |

medicines. They work nationally and collaborate internationally to monitor and identify the harm caused by medicines, to reduce the risks to patients and to establish worldwide pharmacovigilance standards and systems.

## 4. ROLES & RESPONSIBILITIES

4.1. The following are key roles and responsibilities in this document:

| Title | Description of Roles and Responsibilities |
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| HCPs | Diagnose, manage, document and report ADRs and other health product related issues to the NRA. |
| HCRs | Ensure the safety and efficacy of any products they manufacture, import or distribute and sell in the South African market and must comply with all legislative and regulatory requirements of the country. |
| Public Health Programmes | Supports SAHPRA in monitoring AEs and other medicine safety-related issues through the NPC-PHP and the EPI. The NPC-PHP is responsible for monitoring medicines employed in the public health programmes, particularly for HIV and TB, while the EPI is concerned with vaccines, for both children and adults.<br>Capacity-building activities for HCPs, policy development (including developing guidelines for pharmacovigilance), and risk communication for the concerned programmes. |
| NISEC/PISEC | Perform causality assessment on all serious and severe AEFIs submitted to the EPI and SAHPRA, to determine a causal relationship between the vaccine and the vaccine. The PISEC perform pre-liminary causality assessment which is shared with NISEC for finalisation. |
| NPvSC | Strengthen coordination and collaboration between SAHPRA, national and provincial health authorities to standardise pharmacovigilance structures, systems and ADR reporting tools in South Africa. |
| NPVWG | Implement the decisions made by the NPvSC in relation to PV strengthening, coordination, collaboration, harmonisation and awareness activities. |
| Patients and Consumers | Consumers offer first-hand information about their experiences with medicines and how the adverse effects affect their lives, and are therefore responsible to inform their HCP or report directly to the NRA |
| Pharmacovigilance Advisory Committee | Review and make recommendations to the NRA on issues related to medicines' safety. |

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| PTCs | Implementing bodies of medicine-related governance in the provinces, districts and health establishments, responsible for identification, investigation and management of medicine use problems and promotion of strategies to improve medicine use and patient safety. |

## 5. RELATED INFORMATION AND DOCUMENTS

5.1. The following references are used:

| Title | Document Number | Applicable Clause / Section |
|---|---|---|
| Medicines and Related Substance Act, | Act 101 of 1965 as amended | Section 2B |
| Regulations to Medicines Act | Regulations | Regulation 40 |

## 6. CONTENT

### 6.1. Introduction

According to the Medicines and Related Substance Act, 1965 (Act 101 of 1965) as amended, the South African Health Products Regulatory Authority (SAHPRA) has the mandate to ensure that all health products available in the country are of acceptable safety, quality, efficacy and performance. The safety, quality, and efficacy of health products are essential to protecting public health and maintaining trust in healthcare systems. However, no health product is entirely risk-free as adverse events can occur even after rigorous pre-marketing evaluation through clinical trials. For this reason, the Authority has developed a national health product vigilance framework to provide a structured, coordinated and collaborative approach to monitoring, detecting, and responding to safety concerns associated with health products throughout their lifecycle.

A national vigilance framework enables the timely identification of safety concerns, facilitates regulatory action, and supports evidence-based decision-making by healthcare professionals and policymakers. This framework establishes systematic processes for detecting, assessing, understanding, and preventing adverse effects or problems related to the use of health products in South Africa. The desired outcomes include enhanced patient safety, regulatory oversight, public

confidence and global alignment. By preventing health product related adverse events, a strengthened vigilance system reduces the economic and resource burden on health services, thus improving healthcare system efficiency. Therefore, this framework is not only a regulatory requirement but also a public health imperative. It provides the foundation for a proactive, responsive, and transparent approach to safeguarding public health, ensuring that the benefits of health products consistently outweigh their risks throughout their lifecycle.

### 6.2. Background

In 2020, SAHPRA, in pursuance of a more strengthened regulatory system underwent assessment by the World Health Organisation (WHO) Global Benchmarking Tool (GBT), with the anticipation to attain Maturity Level 3 for both medicines and vaccines. However, SAHPRA only attained GBT Maturity Level (ML) 3 for vaccines. This was due to the effective coordination of pharmacovigilance activities between the Expanded Programme on Immunisation (EPI) within the National Department of Health (NDoH) and SAHPRA, which was further enhanced by the well-coordinated response to the COVID-19 pandemic.

In contrast, pharmacovigilance activities for medicines were co-managed by two entities, SAHPRA and the National Pharmacovigilance Centre for Public Health Programmes (NPC-PHPs) within the NDoH. The Pharmacovigilance unit within SAHPRA was responsible for monitoring the safety performance of all medicines available on the South African market, while the NPC-PHPs focused on surveillance of medicines used within public health programmes e.g. HIV/AIDS and tuberculosis (TB). The lack of centralisation of pharmacovigilance oversight led to poor co-ordination of pharmacovigilance activities between the two organisations, resulting with duplication of efforts and confusion among HCPs on where to report ADRs. As a result, SAHPRA attained ML2 for medicines. Since then, SAHPRA has taken measures to lead and harmonise pharmacovigilance activities within the country, based on the WHO's recommendations. The aim is to have a co-ordinated, centralised vigilance database that integrates hospital, clinic, and programme-level data.

A robust co-ordinated national health product vigilance system is not only key to achieving higher regulatory maturity levels within the WHO GBT framework, but to also ensure consistent ADR reporting across provinces and facilities and establish clear standard operating procedures and guidelines that all health institutions follow. This is important to strengthen regulatory capacity,

optimise benefit-risk information for regulatory decision making, and for optimal health outcomes for the South African population.

### 6.3. Legal Basis for the National Vigilance Framework in South Africa

Vigilance in relation to a medicine, medical device or IVD, means the continuous monitoring and evaluation of its safety, efficacy, quality and performance profile and, the management of any risk throughout its life cycle. Regulation 40 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965), as amended mandates that:

(1) An HCR in terms of section 15 of the Act or a holder of a license 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

(a) new or existing quality, safety or effectiveness concerns related to any medicine or scheduled substance, including but not limited to adverse drug reactions; and

(b) risk management activities associated with paragraph (a).

(2) An HCR in terms of section 15 of the Act or a holder of a license in terms of section 22C (1) (b) must maintain or have access to records of the reports and case reports referred to in sub regulation (1) above.

(3) An HCP, 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.

This vigilance legislation aims to improve vigilance awareness and ensure that evidence of existing and new AEs emerging from post-marketing surveillance and vigilance activities are investigated, monitored, analysed and acted upon.

### 6.4. Guiding Principles of health Product Vigilance in South Africa

The framework is based on the following guiding principles:

- Standardisation and harmonisation of vigilance activities, systems and structures throughout the country.
- Application of health product vigilance principles and practice in both private and public healthcare systems at all levels to ensure patient safety.
- Patients must have access to safe and effective health products.

- HCPs must consider health product vigilance practices as a professional responsibility.
- Existence of consistent and effective partnerships and enhanced collaboration and engagement with all vigilance stakeholders.
- Use of current WHO and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines for different types or methods of health product vigilance activities including causality assessment and pharmacovigilance training tools.
- Collection of ADRs/AEFIs in an ethical and confidential manner and analysis and communication of safety information in a way that improves therapeutics and patient safety
- Utilise scientific methods e.g., epidemiological studies, to generate safety and efficacy data where necessary to support decision making.

## 7. Shared Responsibilities for Health Product Vigilance Framework

The maintenance and improvement of health and safety is understood to be a shared responsibility that requires a collective effort at all levels of the health system. In addition to the government and pharmaceutical companies, other stakeholders such as HCPs, patients, consumers and their respective associations play an important role in identifying, reporting and addressing health product safety related issues.

### 7.1. South African Health Products Regulatory Authority (SAHPRA)

The Authority, as a regulatory body, is responsible for overseeing the safety of all health products, including pharmaceuticals, complementary health products, radiation-emitting devices, medical devices, IVDs, cannabis products, and other controlled substances. It also manages health risks associated with environmental contaminants. The Authority is therefore responsible for protecting and advancing the health of the South African public. This includes strengthening health product vigilance through provision of more effective and efficient surveillance practices, increased transparency and greater accountability and performance reporting via process improvements.

A further responsibility of the Authority is to ensure that the health products vigilance system is operational and that methods are in place to receive and manage vigilance data, monitor and evaluate that data, and manage the risks. The South African vigilance system is designed to ensure early detection of health product-related AEs, as well as detection of previously unknown adverse reactions (signals). SAHPRA has a Pharmacovigilance unit that ensures that the vigilance system functions as it is intended to.

SAHPRA is responsible for the regulatory oversight of HCRs including the development, implementation and enforcement of legislative and regulatory controls, and maintains up-to-date safety information on health products which is communicated through various means to HCPs, patients and consumers. For marketed health products, post-authorisation safety data is highly dependent on the submission of AE reports and new significant safety information by applicants/HCRs and HCPs, within specific time frames as determined by the Authority. Submission of this information is important because the use of a health product changes over time, under real-world conditions, and therefore allows for a more accurate understanding of its benefit-risk profile. SAHPRA aims to improve the integration of this new safety information into the benefit-risk profiles of the products on an ongoing basis, throughout the life cycle of the products] to improve medicines prescribing and use outcomes.

The Authority also aims to minimise the risks associated with the use of health products through the conduct of good vigilance practice inspections, training of HCPs and the public, conduct of safety related studies that assist in the identification of medicine safety issues and reliance on globally recognised regulatory authorities (RRAs) with robust vigilance systems and regulatory processes.

### 7.2. World Health Organisation – Uppsala Monitoring Centre

The WHO PIDM is an international collaboration with the goal to ensure identification of medicines and vaccine-related safety issues. The UMC is the WHO Collaborating Centre for International Drug Monitoring and provides support to programme members to establish and develop national systems for monitoring the safety of medicines. It is responsible for managing the technical and scientific aspects of the WHO's worldwide pharmacovigilance network. The UMC has been responsible for the technical and operational activities of the PIDM since 1978. The activities include:

a) Collecting, assessing and communicating information from member countries about the benefits, harms, effectiveness and risks of medicines.
b) Analysing VigiBase® (WHO global database for safety reports submitted by participating members) data and identifying signals of potential safety problems.
c) Collaborating with member countries in the development and practice of pharmacovigilance through consultation and training.
d) Pursuing research in all aspects of the science and practice of pharmacovigilance.
e) Broadening the scope of pharmacovigilance through debate, research and consultation.
f) Being a partner in the extended global patient safety network.

g) Developing and providing tailored data-entry, management, retrieval and analysis tools such as VigiFlow® and VigiLyze®.
h) Providing and maintaining the WHO Drug Dictionary portfolio and the WHO Adverse Reactions Terminology (WHO-ART) used for coding and analysis of VigiBase® and health product data throughout the world.

### 7.3. National Department of Health – Public Health Programmes

Public health programmes serve to promote health and prevent the spread of diseases, premature death, and disease-related discomfort and disability in the population. Through the PHPs, large populations receive medicines for diseases such as HIV, TB, and malaria, as well as vaccines and sexual and reproductive health products. This necessitates intensive monitoring of AEs associated with medicines used in these programmes.

The NDoH supports SAHPRA in monitoring AEs and other medicine safety-related issues through the NPC-PHP and the EPI. The NPC-PHP is responsible for monitoring medicines employed in the public health programmes, particularly for HIV and TB, while the EPI is concerned with vaccines, for both children and adults. They are involved in capacity-building activities for HCPs, policy development (including developing guidelines for pharmacovigilance), signal detection, and risk communication for the concerned programmes. Active pharmacovigilance must be undertaken by all PHPs who use medicines because no medicine is without adverse consequences, although these vary in severity and frequency. Treatment guidelines and protocols used by PHPs should include instructions on reporting ADRs.

PHPs sometimes do not always collaborate with the NRA, leading to duplication of effort and a lack of harmonised terminologies, data collection methods, and causality assessment. The collected information may not be added to VigiBase®, and as such, the international community does not benefit from it. This highlights the need for a more harmonised approach for all national vigilance activities, which SAHPRA has embarked on.

### 7.4. Holders of Certificate of Registration (HCRs)

The HCRs or applicants have the primary responsibility of ensuring the safety and efficacy of any products they manufacture, import or distribute and sell in the South African market and must comply with all legislative and regulatory requirements of the country. Companies must have an internal

pharmacovigilance system in place and be responsible for the safety monitoring of their registered health products in South Africa. The HCR should ensure that information on ADRs is collected, collated and communicated to SAHPRA. The HCRs must report promptly to SAHPRA, any new significant safety information relating to their registered products, in alignment with the 'Post-Marketing Reporting of Adverse Drug Reactions (ADRs) for Human Use in South Africa' guideline. Additionally, HCRs are mandated to have qualified person for pharmacovigilance (QPPV) who is responsible for the PV system as outlined in the 'Pharmacovigilance systems guideline'.

### 7.5. Healthcare Professionals

Although the regulation of medical professions does not fall under the regulatory authority, HCPs play an important role in monitoring the real-world safety of health products by reporting safety information to SAHPRA or to HCRs/applicants on a voluntary basis through spontaneous reporting. Healthcare professionals are encouraged to inform SAHPRA of any problems they encounter with marketed health products. Healthcare professionals also share responsibility for the safe use of products prescribed for their patients. Essential roles of HCPs in the national vigilance system are to:

- Diagnose, manage, document and report ADRs and other health product related issues to the NRA.
- Ensure that risks in medicine use are anticipated and managed.
- Provide regulators with the necessary information to amend the recommendations on the use of health products.
- Improve communication between the HCPs and the public.
- Educate patients on the safe use of health products and help them understand the benefits and risks of health products that are prescribed for them.

### 7.6. Patients and Consumers

Direct patient reporting of suspected AEs can provide valuable information for monitoring the safety of health products. Patient reports are usually more detailed and explicit compared to reports from HCPs. Consumers can offer first-hand information about their experiences with medicines and how the adverse effects affect their lives. Allowing the public to report ADRs directly to the authorities is an alternative way to increase ADR reporting as consumer reports can complement HCP reports by identifying potential new ADRs and contributing to reliable monitoring systems. Consumer reporting can be important in helping individual patients receive optimal therapy and safeguard PHPs.

### 7.7. Committees and working Groups Supporting Vigilance Activities in South Africa

There are several committees that support vigilance activities in South Africa through providing expert guidance, guideline development and strengthening vigilance processes at national, provincial, district and health facility levels.

#### 7.7.1. The Pharmacovigilance Advisory Committee

The Pharmacovigilance Technical Advisory Committee is composed of multidisciplinary experts in various fields such as vaccinology, paediatrics, complementary medicines, clinical pharmacology, pharmacovigilance, academia etc. The general objective of the Committee is to support the monitoring of the benefit-risk balance in relation to the human use of any medicine to which any provision of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) applies. The Committee provides advice, in the form of recommendations, to the Authority on matters referred to it or on such matters relating to:

a) The ongoing benefit-risk assessment of medicines during the post-marketing phase;
b) New safety signals from local data or shared by other NRAs and
c) Vigilance activities, including ADR reporting in South Africa.

#### 7.7.2. The National Pharmacovigilance Steering Committee

To improve harmonisation of vigilance activities in South Africa, the Authority together with the representatives from the NPC, the EPI Directorate and Heads of Pharmaceutical Services from all provinces established the National Pharmacovigilance Steering Committee (NPvSC). The purpose of the NPvSC is to strengthen coordination and collaboration between SAHPRA, national and provincial health authorities to standardise pharmacovigilance structures, systems and ADR reporting tools in South Africa and to improve pharmacovigilance awareness and education among HCPs through training and capacity building initiatives.

#### 7.7.3. The National Pharmacovigilance Working Group

The Working Group is a sub-entity of the NPvSC made up of PV leads or champions from the authority, NDoH, and provinces responsible for implementing the decisions made by the Steering Committee.

#### 7.7.4. The National and Provincial Immunisation Safety Expert Committees

The National Immunisation Safety Expert Committee (NISEC) is a non-statutory, ministerial appointed advisory committee of independent experts. The Committee is responsible for causality assessment

of all serious and severe AEFIs submitted to the EPI and SAHPRA, to determine whether the event may have been caused by the vaccine or whether it was coincidental. The main purpose of NISEC is to provide, independent, authoritative, scientific advice and recommendations to the NDoH and the National Advisory Group on Immunisation.

The NISEC also supports the establishment and strengthening of Provincial Immunisation Safety and Expert Committees (PISECs) in different provinces. Where available, PISECs coordinate the assessment of AEFIs reported in their respective provinces and submit their preliminary assessments to NISEC for further assessment and finalisation.

#### 7.7.5. Pharmaceutical and Therapeutics Committees

Pharmaceutical and Therapeutics Committees (PTCs) are the primary implementing bodies of medicine-related governance in the provinces, districts and health establishments in South Africa. Functional PTCs contribute to improved quality of patient care and health outcomes. Their roles and functions in health product vigilance and patient safety include:

- Regular review of ADR reports and informing HCPs of the incidences and impact of ADRs in the region or hospital of their jurisdiction.
- Discussing changes in the formulary or standard treatment guidelines due to significant or recurring health product related problems.
- Educating staff, especially HCPs on ADRs and rational medicine use.
- Identifying “high risk” medicines on the formulary that require close monitoring by HCPs.
- Identifying “high-risk” patient populations, including pregnant and breastfeeding women, the elderly, children, and patients with renal or liver dysfunction for close monitoring of these patient populations to prevent or minimise serious ADRs.
- Reviewing medication errors and product quality complaints to ensure they are not contributing to the health facility's ADR incidence.

### 7.8. Partnerships, Alliances and Collaboration

Partnerships, alliances and collaboration are key to improving and advancing South Africa's national vigilance system. These partnerships and collaborations can directly or indirectly facilitate the development and sustainability of a robust health product vigilance system.

#### 7.8.1. Medicine Information Centres

South Africa has a Medicine Information Centre (MIC) in the Western Cape province which provides medicine information to HCPs. The MIC is also a centre of excellence for pharmacovigilance active in the province that produces quarterly and annual reports on medicine safety issues.

### 7.8.2. Non-governmental organisations

These provide support to the national pharmacovigilance system through:

i. Capacity-building
ii. Health systems strengthening
iii. Mentorship
iv. Providing resources

### 7.8.3. Academia

Academia plays a significant role in health product vigilance through various activities. This includes conducting in-depth research, providing comprehensive training programmes, and integrating health product vigilance education into the undergraduate and postgraduate curricula for relevant qualifications at South African universities. Additionally, academia actively collaborates with regulatory authorities and pharmaceutical companies, including serving on advisory committees, working groups and boards.

### 7.8.4. Health Professional Associations

Medical, pharmacy, nursing and other associations can educate their members through continuous professional development seminars on medicine safety. They also play a key role in the dissemination of medicine safety information and in influencing policy and practice of pharmacovigilance.

### 7.8.5. Advocacy groups

In many instances, these organisations have the capacity to voice and often change public opinion. Their roles include**:**

i. Public sensitisation on medicine safety
ii. Facilitating active public debate and discussion of issues which have direct relevance to health
iii. Highlighting deficiencies and weaknesses in existing medicine safety policies
iv. Engaging proactively with policymakers on essential matters of public interest to facilitate the creation of policies and legislation on pharmacovigilance.

### 7.8.6. Media

Media play a major role in dissemination of information to the public and in influencing public perception about the safe use of medicine. Effective media engagement can help foster public trust in the regulatory authority.

## 8. The Health Product Vigilance System for South Africa

The patterns of how people access and use health products are changing because of globalisation, free trade, and increased use of the internet. These changing patterns require vigilance activities to be more closely linked and therefore better able to respond to how health products are being used in society.

South Africa operates in an increasingly complex environment influenced by a number of factors, such as public expectations and awareness, evolving science and technology, the global regulatory environment and government priorities. These factors influence how SAHPRA carries out its mandate and delivers programmes and services to meet the evolving needs of the South African public. These factors reinforce the need for coordinated action, partnership and collaboration in the health product vigilance system.

## 9. Mechanisms and Tools for the Collection and Analysis of Vigilance Data

At present, there are innovations in vigilance tools and technologies that support the development, integration and use of these tools. SAHPRA's current product vigilance system is composed of tools that are anchored by regulations describing the responsibilities of the HCRs and the Authority for collection, analysis, and decision-making and sharing of vigilance data. This framework describes the vigilance tools and explains how they function within South Africa. Data that is generated is used to re-evaluate the benefit-risk profile of marketed products and to make decisions about their continued certificate of registration. SAHPRA will update this framework periodically as new vigilance tools are developed and integrated into the health product vigilance system.

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vigilance tools and explains how they function within South Africa. Data that is generated is used to re-evaluate the benefit-risk profile of marketed products and to make decisions about their continued certificate of registration. SAHPRA will update this framework periodically as new vigilance tools are developed and integrated into the health product vigilance system.

### 9.1.1. Adverse Event Reporting

Reports on adverse effects of all health products used in South Africa must be submitted to SAHPRA by HCRs/applicants, HCPs and the public, including for use in unapproved indications. For marketed health products, HCRs/applicants are required to submit individual case safety reports (ICSRs), including reports of lack of efficacy and further inform the Authority of any identified new safety issues. Reporting of adverse reactions and their monitoring remains a viable means of identifying previously unrecognised rare or serious adverse reactions.

#### (a) Spontaneous Reporting

As part of post-marketing surveillance, SAHPRA collects information on ADRs/AEFIs through spontaneous reporting. Spontaneous reporting is considered the backbone for the existence of a vigilance system. Spontaneous reporting is by nature a passive approach to pharmacovigilance, relying entirely on the motivation of individuals to report suspected ADRs to the Authority. An important feature of spontaneous reporting is that it covers all health products used within a whole population for an unlimited period, encompassing the entire product life cycle of each health product.

#### (b) Reporting Tools

Electronic and manual reporting tools are available for the reporting of adverse reactions. Reporting tools used by the Authority for spontaneous reporting include:

- Paper-based or manual forms for both medicines ( https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/) and vaccines (https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/) , submitted to a dedicated mailbox (adr@sahpra.org.za);
- Electronic E2B reports submitted by HCRs to a dedicated mailbox (e2b@sahpra.org.za);
- e-Reporting portal available on the SAHPRA website (https://vigiflow-eforms.who-umc.org/za/ereporting)
- Med Safety App (Medsafety X SAHPRA)

- VigiMobile App for reporting AEFIs

**(c) Reporting guidelines**

The success of SAHPRA's reporting systems depends on the quality, completeness and accuracy of the data collected and the analysis thereof. The following guidance documents exist for the mandatory reporting of ADRs by HCRs/applicants to SAHPRA, and are available on the SAHPRA website:

- Post-Marketing Reporting of ADRs to Human Medicines in South Africa
- Pharmacovigilance Systems Guideline
- Pharmacovigilance inspections guideline

In addition to the above, SAHPRA has the following reporting guidelines that guides and support the reporting by the HCPs, and are available on the SAHPRA website:

- Guideline for ADR reporting for healthcare professionals
- Vaccine safety surveillance manual in South Africa

**(d) Reporting of Serious Adverse Events During Clinical Trials**

During a clinical trial, whether prior to or following marketing of a product, the sponsor of a SAHPRA-authorised clinical trial, is required to inform the Authority of any suspected unexpected serious adverse reactions that occurred inside or outside the country. This information allows timely identification of safety signals of health products in clinical trials (whether in development or already marketed) and aids in the identification of safety signals and the development of risk management plans (RMPs).

Clinical trial sponsors are inspected to ensure the trials are conducted according to good clinical practice (GCP) guidelines. The inspection does not cover all trials, but only a representative sample of clinical trial sponsors (Phase I-III Studies) to ensure the trials are conducted under GCP guidelines, in line with international practices. Phase IV studies are subject to post-marketing ADR reporting requirements.

**(e) Centralised Database for Individual Case Safety Report Management**

South Africa became a member of the WHO PIDM in 1992 and therefore acquired the WHO reports management system, VigiFlow®. The VigiFlow® supports the domestic collection and processing of ICSR data and sharing of reports with VigiBase®, which is the global database of adverse event reports submitted by PIDM member countries. The VigiFlow® system further allows electronic submission of ICSRs by HCRs using the ICH E2B format. The system permits maximum local control and provides

effective means for management review and analysis of national data through VigiLyze®. The WHO has therefore provided the public access to the information on the VigiBase® through VigiAccess®.

**(f) Vigilance Hub**

The Vigilance Hub is the back-end system of the Med Safety App used for reporting ADRs and is offered by the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom. The Vigilance Hub allows a user to view all submitted reports, from the Med Safety App and other linked channels. Reports entered into or updated within the Vigilance Hub are updated in VigiFlow®.

### 9.1.2. Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs)

In accordance with the guideline for *Post-Marketing Reporting of ADRs to Human Medicines in South Africa*, HCRs/applicants are required to notify the Authority of a significant change in a product's benefit-risk profile and provide an overall safety evaluation of the product in the form of an annual summary report. Based on the outcome of the review of the change in the benefit-risk profile of a health product, the Authority may request case reports of all ADRs and an evaluation of the product's safety profile. When such a request is made, HCRs/applicants must submit a PSUR/PBRER to SAHPRA for further assessment and decision-making.

Furthermore, a PSUR/PBRER may be requested for submission as a condition of registration for close monitoring of high-risk health products. Alternatively, these reports are to be prepared by HCR/applicant as determined by the European Union Reference Dates (EURD) list (Refer to the Post-Marketing Reporting of ADRs to Human Medicines in South Africa guidelines, for further information on PSURs/PBRERs).

### 9.1.3. Risk Management Plan

An RMP is a dynamic, stand-alone document reflecting both known and emerging safety data (i.e., non-clinical and clinical) that is updated throughout the medicine's life cycle. It describes a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent, or minimise risks related to a specific medicine and, the assessment of the effectiveness of those interventions. All registered medicines require an RMP, but additional requirements may be imposed as conditions of registration. The RMP is an integral part of the electronic Common Technical Document (eCTD) submitted as an application for registration of a medicine.

SAHPRA has an RMP guidance document, *Risk Management Plans for Medicines for Human Use* ***(SAHGL-CEM-PV-03)*** which was implemented since September 2022. SAHPRA receives and reviews risk management plans from HCRs/applicants as determined by this guideline.

### 9.1.4. Pharmacovigilance Inspections

SAHPRA has a Pharmacovigilance Inspection and Systems Guidelines, implemented for the purpose of assessing and verifying compliance of applicants with the Medicines Act regarding the regulatory requirements pertaining to the reporting of ADRs and reporting of unusual failure in efficacy of new medicines. The guidance documents are applicable to all HCRs.

## 10. Signal Detection and Benefit-Risk Assessment of Health Products

New safety signals can be detected from several sources, including spontaneous reports, scientific literature and publications, clinical trials, safety databases, mass media, and social media. Whatever source of safety data is used, detecting signals ought to follow a systematic method and be adequately documented. Qualitative and quantitative methods are used for signal detection. Once a signal has been detected the relationship between a health product and the occurrence of an adverse effect is further evaluated to decide if any regulatory action or risk minimisation measures are required.

Benefit risk assessment is an ongoing process of evaluating a health product's potential positive effects (benefits) against its potential risks. The assessment uses data from various sources such as ICSR reports, RMPs, PSURs and other safety information submitted by applicants or identified from other regulatory authorities. This is important to determine whether the product's benefit outweighs the risks for a specific population or individual.

## 11. Risk Management

The Authority considers various strategies to minimise or prevent harm to the public based on identified risks for a specific health product. This is dependent on the nature, seriousness and public health impact of the identified risk and may include one or more of the following methods:

- Targeted safety studies or surveillance systems (e.g., patient registries for high-risk products, targeted spontaneous reporting)
- Product labelling changes, including new warnings, changes in scheduling status, packaging and improved manufacturing

- Safety communication
- Market withdrawal or product recall

## 12. Reporting and Communication on Health Product Vigilance Activities

SAHPRA provides feedback on the monitoring and evaluation of information related to the safety and efficacy of marketed health products through a variety of means which include the following:

- Safety communication to disseminate new safety information and communicate appropriate risk minimisation measures through various communication channels. The communication may be disseminated to HCPs and the public.
- Communication to HCRs with regulatory decisions and recommendations for specific health product related issues. Any action required from the applicant will be communicated with specific timelines for implementation.
- Data is shared with local and global collaborating partners through formal and informal reports disseminated through meetings and emails.
- Publication of vigilance information through the Medi-Guardian newsletter and the quarterly summary of medicine safety regulatory decisions published on the SAHPRA website and accessible to HCRs, HCPs and the public.

### 12.1. Safety Communication

SAHPRA aims to provide timely, evidence-based information in the safe use of medicines. SAHPRA has a *Vigilance Risk Communication Framework* that provides a strategic approach for effective communication of important safety information to all stakeholders within the vigilance system. The Authority's safety communication strategy is guided by the following principles:

- There should be adequate coordination and cooperation between the different parties involved in issuing safety communication (e.g., HCRs).
- Safety communication should be subject to quality controls to ensure accuracy and clarity.
- Safety communication should deliver relevant, clear, accurate and consistent messages and should reach the right audiences at the right time for them to take appropriate action.
- Safety communication should be tailored to the appropriate audiences by using appropriate language and taking account of the different levels of knowledge and information needs whilst maintaining the accuracy and consistency of the information conveyed.

### 12.2. Communication tools and channels

The communication tools and channels used by the Authority include:

- Dear healthcare professional letters.
- Media releases and briefings.
- Notification on the website of the regulatory authority.
- Med Safety App, social media and other online communications.
- Bulletins and newsletters.
- Responding to enquiries from the public, HCPs and HCRs.
- Publications in scientific journals and journals of professional bodies.

## 13. STRATEGIES TO OPTIMISE AND STRENGTHENING THE HEALTH PRODUCTS VIGILANCE SYSTEM

The Authority strives to improve the health product vigilance system through the harmonisation of vigilance activities in the country and the continuous integration of new health product vigilance tools for information gathering and processing, monitoring and evaluation and risk management.

It is expected that the comprehensive system encompasses monitoring of medication errors and therapeutic ineffectiveness (due to poor treatment adherence, antimicrobial resistance, product quality problems, inappropriate use, or interactions); product quality problems; vigilance of other health products (medical device and IVDs) and communication of such information to HCPs and consumers on risk-benefit decisions.

The harmonised vigilance system is built on the current system of collection, analysis, decision-making and sharing of vigilance data. The Authority's desire is to expand the current vigilance system from a passive ADR surveillance model that relies on voluntary reports from HCPs or consumers to incorporate active surveillance methods to address priority safety concerns, such as the use of registries, sentinel sites, and follow-up of defined patient cohorts. Active surveillance and other forms of proactive vigilance will support decision-making by providing information that is more opportune, more complete and of better quality.

### 13.1. Decentralised Health Product Vigilance System

Traditionally, a vigilance system is strongly centralised and consists of one national centre collecting reports from HCPs around the country. However, SAHPRA is has moved towards a more decentralised

system with the NRA functioning as the focal point for programmatic, provincial and facility-based centres as depicted in **Figure 1.** This is because vigilance activities are carried out at all levels of health services and require collaborative action and standardised practices. The decentralised vigilance system incorporates activities and resources at the facility, provincial, national, and international levels and foster collaboration among a wide range of partners and organisations that contribute to ensuring health products safety.

Figure 1: The hierarchical structure of a decentralised health product vigilance system

The vigilance collaboration initiative between PHPs and the Authority facilitates sharing of expertise, experience and resources and standardise data collection methods and reporting tools. The outcomes of this collaboration are:

- Improved coordination of safety reporting and case management for vaccines and therapeutics by aligning provincial ADR/AE reporting procedures and practices to SAHPRA guidelines and monitoring compliance with implementation.
- Accessibility to functional vigilance tools for safety reporting and monitoring of AEs at all levels of the healthcare structure.
- Establishment of the safety expert committees for vaccines and therapeutics and provision of support for decentralised investigation, assessment and management of ADRs/AEs, while providing technical support to ensure their functionality at the provinces.
- Strengthened pharmacovigilance awareness and knowledge through targeted training and capacity building of HCPs and other stakeholders, central to vigilance activities.

In addition to a decentralised approach, the authority has identified strategies to optimise and strengthen the national health product vigilance system. These strategies are also intended to address critical challenges and barriers to an optimal health product vigilance system such as fragmented vigilance processes and activities, underreporting of adverse effects especially at primary care level, suboptimal use of technological innovations and poor availability of trained personnel at all levels of care.

### 13.2. Leverage emerging technologies to strengthen vigilance activities

Vigilance is a data driven process and relies on information systems to extract data to conduct appropriate health product safety surveillance, so new technologies can facilitate real time data collection and analysis from diverse sources and large data sets. This allows for the early detection of

safety signals, the detection of patterns of AEs as well as provide refined risk assessment tools. Technology can also enable the Authority to detect AEs that cannot be easily identified through traditional reporting methods to support patient centred safety monitoring. This allows the Authority to respond faster to safety concerns, and enhance regulatory compliance and decision-making using technological advancements, while moving towards a more proactive and adaptive approach to monitoring the safety of health products used in South Africa.

### 13.3. Establish Active Surveillance Systems

Active surveillance systems provide the ability to detect, assess, and respond to AEs associated with health products in real time. South Africa's unique health context necessitates tailored vigilance mechanisms. The country's high prevalence of HIV, TB, and emerging non-communicable diseases has resulted in widespread use of complex treatment regimens, often involving multiple products used concurrently. Active surveillance provides context-specific evidence on product safety and effectiveness in the South African population, where genetic, epidemiological, and socio-economic factors may differ from those in other countries.

Active surveillance improves the responsiveness and credibility of regulatory processes, thereby aligning with international best practices. The establishment of active surveillance systems for health products vigilance in South Africa is essential to protect patient safety, strengthen regulatory decision making, build public trust, and enhance global collaboration and support the sustainability of the national health product vigilance system.

### 13.4. Strengthen benefit-risk assessment capacity

Strengthening benefit-risk assessment capacity is essential to ensure that health products remain safe, effective, and aligned with public health priorities, as health technologies evolve and global markets expand. Building benefit-risk assessment capacity enhances the quality and timeliness of regulatory decisions, allowing authorities to act swiftly when new safety signals arise. It supports transparent, evidence-based communication with health professionals and the public, fostering trust in the regulatory system. Strong benefit–risk assessment frameworks also promote consistency in decision-making, minimise preventable harm, and optimise therapeutic value for patients.

Capacity strengthening can be achieved through investment in skilled multidisciplinary teams, robust data infrastructure for real-world evidence, and standardised methodologies for comparative

assessment. International collaboration and knowledge-sharing further ensure that resource-limited settings can adopt best practices while tailoring them to local health needs. Biostatistics, pharmacoepidemiology, and data science are central to building robust benefit–risk assessment capacity for health product vigilance. Strengthening these disciplines will improve the accuracy, timeliness, and contextual relevance of risk detection and benefit quantification.

### 13.5. Strengthen Reporting at the Patient and Consumer Level

The Authority regards consumer reports to be a valuable contribution in monitoring the safety of medicines. Although consumer reporting has been implemented with Med Safety App and e-Reporting, there is a need to empower consumers about medicine safety awareness and the need to reporting. Empowerment will be done in different mechanisms including translation of the App into five local languages (Afrikaans, Zulu, Sesotho, Venda and Tsonga), to promote the uptake and reporting of ADRs by patients/consumers, webinars, campaigns, etc.

### 13.6. Adopt a product lifecycle approach

It is well recognised that product vigilance needs to occur throughout a health product's life cycle. This National Pharmacovigilance Framework considers vigilance as it relates to the entire product life cycle and will require regulatory change for some elements. Regulatory agencies around the world are continuously building on the strengths of the pre-marketing review and adopting a life cycle approach that considers the body of evidence that accumulates throughout the life cycle of the product and have therefore enacted the necessary legislation to support this shift.

### 13.7. Align with international best practices and standards

SAHPRA has committed to aligning its regulatory approaches related to product vigilance, wherever possible, with those of comparable international regulatory counterparts. This includes a commitment to full integration of ICH vigilance tools and provides the vehicle through which international work and information sharing can proceed.

### 13.8. Facilitate industry compliance with vigilance best practices

Through the development of this framework, SAHPRA will provide regulated pharmaceutical industry with the tools needed to follow vigilance best practices. This will include an explanation of the various vigilance tools, when they are used, and appropriate guidance to facilitate compliance with the tools.

### 13.9. Adopt key vigilance components

The Authority's health product vigilance activities will be guided by four key principles which are transparency, timely decision-making, use of precautionary approach, and meaningful public involvement.

### 13.10. Continuously improve health products vigilance

SAHPRA recognises that product vigilance activities may change over time as knowledge of products evolve. A product's vigilance requirements will be subject to review over a product's life cycle, on the basis of the evolution of knowledge, technology and society's chosen level of protection. In addition, vigilance tools will be evaluated for effectiveness in achieving desired outcomes.

### 13.11. Uphold product efficacy and safety standards

The requirement for specific vigilance activities is for the purpose of protecting the health and safety of South Africans and will in no way result in the reduction in a product's requisite efficacy and safety standards.

### 13.12. Strengthening SAHPRA's Regulatory Reliance Approach

Given limited resources, and the need for timely regulatory decisions, strengthening SAHPRA's regulatory reliance approach is an essential mechanism for optimising health product vigilance in South Africa. The Authority already considers trusted international evaluations by RRAs such as the United States Food and Drug Administration, the European Medicines Agency, the Australian Therapeutic Goods Administration, the MHRA, Health Canada, Japan's Pharmaceuticals and Medical Devices Agency and the WHO prequalification programme. Regulatory reliance fosters learning from the scientific and regulatory expertise of established authorities, supporting the continuous development of regulatory science in South Africa.

Regulatory reliance improves efficiency by reducing unnecessary duplication of work and aligns the country with international regulatory best practices, while allowing SAHPRA to focus its resources on other local public health priorities and post-market surveillance. By drawing on existing regulatory intelligence, SAHPRA can respond more rapidly to emerging safety issues and ensure that products available in South Africa meet global benchmarks for quality and safety.

## 14. FRAMEWORK AUTHORISATION

14.1. The Framework Owner/ Manager is responsible for the maintenance and review of this Framework. This Framework will be reviewed every 3 years or when the need arises.

**Framework Owner:** Ms Florah Matlala (PV Manager)

**Framework Manager / Cognisant Person:** Electronically signed by: Mahlodi Moropa mahlodi.moropa@sahpra.org.za SIGNIFLOW 23 October 2025

Mahlodi Moropa
(Acting CEM Senior Manager)

Date

**CONFIRMATION OF APPROVAL**

**Approved by:** Tammy Gopal Tammy Gopal SIGNIFLOW 24 October 2025

Ms Tammy Gopal
Name of Executive Member

Date

## 15. ADDENDA

15.1. Addendum A: