The Kingdom of Eswatini

Eswatini National Pharmacovigilance Policy and Implementation Framework

June 2021

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Foreword

The Government of the Kingdom of Eswatini through the Ministry of Health is committed to assure the safety of medicines by promoting pharmacovigilance activities in the country. Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible medicinal product related problems. A rigorous pharmacovigilance system would assist to monitor the safety concerns of medicines, vaccines, blood and blood products, biologicals, herbal medicines, traditional and alternative remedies including food supplements, and oils used in Eswatini.

The National Pharmacovigilance Centre was established in 2009 and became a full member of the WHO Programme for International Drug Monitoring in 2015. The Centre monitors medicinal products with the objective of ensuring the safety of patients and the general public. It therefore gives the Ministry of Health pleasure to present the first edition of the National Pharmacovigilance Policy, which provides policy guidance for the implementation of pharmacovigilance activities in Eswatini. The ultimate goal for such a policy is to optimize medicinal product-related safety for all people living in Eswatini.

This policy was written in-line with current international and local medicinal product safety requirements in consultation with the Ministry of Health (MOH), public health programmes and regional health management team. Stakeholders involved in delivering healthcare in the private sector and the pharmaceutical industry were also consulted.

This policy aims to provide a framework for a national pharmacovigilance system in Eswatini. It also defines the pharmacovigilance activities undertaken by the National Pharmacovigilance Centre and stakeholders. It further delineates the trends and signals of adverse events with medicinal products used in the country and assists policy makers in utilizing evidence-based approaches in patient safety and decision-making related to therapeutics. Lastly, the document outlines the implementation framework of this policy and the stakeholders who play a major role in its implementation in the country. Finally, this policy framework is expected

to inform legislation such as the Medicine and Related Substance Act of 2016, national pharmacovigilance guidelines, standard operational procedures, tools for adverse event reporting and databases used for data management.

It is our hope that both the private and public health sectors set up sustainable pharmacovigilance systems that are coordinated and implemented by and through the National Pharmacovigilance Centre (NPC). I therefore call upon all stakeholders to support the Ministry in the implementation of this policy to ensure the safety of medicinal products in the country.

Honourable Senator Lizzie Nkosi
Minister of Health

Acknowledgements

The development of a pharmacovigilance policy has been an aspiration of the Ministry of Health for the longest time. It is seen as a major step towards not only strengthening the pharmacovigilance system in Eswatini but also as a key aspect of ensuring that the healthcare provided to the Swazi populace is safe and of quality.

The leadership role played by the National Pharmacovigilance Centre, within the Medicines Regulatory Unit of the Ministry of Health, in the compilation of this policy is commendable. The various partners who provided technical and financial support in this process are also appreciated. The Ministry of Health would like to make singular mention of the immense contribution of Pharmacovigilance for Africa (PAVIA), a project supported by the European Union through European & Developing Countries Clinical Trials Partnership (EDCTP), towards the development of this policy. Special mention of other partners like Baylor College of Medicine Children's Foundation Eswatini, Chemonics – the United States Agency for International Development (USAID), Global Health Supply Chain – Procurement and Supply Management (GHSC_PSM), and Clinton Health Access Initiative (CHAI) is also made.

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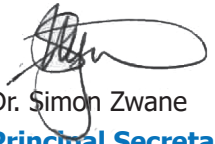

Dr. Simon Zwane
Principal Secretary Ministry of Health

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List of Abbreviations

ADR	Adverse Drug reaction
aDSM	Active TB Drug Safety and Monitoring system
AE	Adverse Event
AEFI	Adverse Event Following Immunization
BLA	Baseline Assessment
CA	Causality Assessment
CEM	Cohort Event Monitoring
DDPS	Deputy Director Pharmaceutical Services
DR-TB	Drug Resistant TB
DUS	Drug Utilization Studies
ENAP	Eswatini National AIDS Programme
EPI	Extended Programme on Immunization
ICH	International Conference on Harmonization
ICSRs	Individual Case Series Reports
MAH	Marketing Authorization Holder
MedDRA	Medical Dictionary for Regulatory Activities
MOH	Ministry of Health
MRU	Medicine Regulatory Unit
NMCP	National Malaria Control Programme
NMRA	National Medicines Regulatory Authority
NPC	National Pharmacovigilance Centre
NPSMC	National Patient Safety and Monitoring Committee
NTCP	National Tuberculosis Control Programme
PBRER	Periodic Benefit Risk Evaluation Report

PHP	Public Health Programmes
PSUR	Periodic Safety Update Report
PTC	Pharmacy & Therapeutics Committee
PV	Pharmacovigilance
RHMTs	Regional Health Management Teams
TB	Tuberculosis
TSR	Targeted Spontaneous Reporting
UMC	Uppsala Monitoring Centre
WHO	World Health Organization
WHO-DD	WHO Drug Dictionary

Definitions of terms

ADVERSE DRUG REACTION (ADR)	A response to a medicinal product, which is noxious and unintended. Adverse reactions may arise from use of the product within or outside the terms of the marketing authorisation or from occupational exposure. Use outside the marketing authorisation includes off-label use, overdose, misuse, abuse and medication errors1.
ADVERSE DRUG REACTION REPORTING FORM	A form designed and distributed by the National Pharmacovigilance Centre (NPC) for reporting ADRs.
ADVERSE EVENT	Any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product2.
CAUSALITY ASSESSMENT	The evaluation of the likelihood that a medicine was the causative agent of an observed adverse event in a specific individual. Causality assessment is usually made according to established algorithms.3
EXPECTED REACTION	An expected ADR is one for which its nature or severity is consistent with that included in the appropriate reference safety information (e.g., Investigator's Brochure for an unapproved investigational product or package insert/ summary of product characteristics for an approved product).
HEALTH PRODUCTS REGULATION	All the processes involved in the pre-marketing evaluation, marketing authorization and post-marketing review of medicines.

1 Guideline on good pharmacovigilance practices (GVP) Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2)

2 ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting

3 Cioms.ch. Published 2021. Accessed May 4, 2021. https://cioms.ch/wp-content/uploads/2021/03/PVGlossary-450x675-1.jpg

HEALTHCARE PROFESSIONAL	A healthcare professional is a qualified person who has acquired the requisite knowledge, skills and competences to deliver proper health care in a systematic way to any individual in need of healthcare services. A health care professional can include physicians, pharmacists, nurses, laboratory technologists, pharmacy technicians, radiographers, etc.
MARKETING AUTHORIZATION HOLDER (MAH)	The holder (an individual, institute, manufacturer, company, importer, distributor, development partner/ donor agency) of a marketing authorization to market a medicinal product. For the purpose of this policy document, the MAHs shall have full responsibility and liability for their product on the market and full responsibility for ensuring that appropriate action can be taken when necessary.
MEDICATION ERRORS	Any preventable events that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer. Such events may be related to professional practice, healthcare products, procedures and systems including prescribing, order communication, product labelling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use.
MEDICINAL PRODUCT	Any substance or product administered to humans for the prevention, diagnosis or treatment of any disease or its symptoms or for the modification of physiological function. In this document, the more globally acceptable definition of medicine is used.
NATIONAL PHARMACOVIGILANCE CENTRE (NPC)	National Pharmacovigilance Centre is a centre that, coordinates pharmacovigilance activities in the country.

PERIODIC SAFETY UPDATE REPORT (PSUR)	A report produced by a MAH intended to provide an update on the worldwide safety experience of a medicinal product to the competent authorities at defined times post authorization.
PHARMACOVIGILANCE	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems4.
POST-MARKETING SURVEILLANCE (PMS)	Monitoring for adverse reactions to marketed products.
REPORTER	Any person who describes a suspected adverse (drug) reaction to the relevant regulatory or competent authority.

4 The Importance of Pharmacovigilance, WHO 2002

SERIOUS ADVERSE EVENT OR REACTION	A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect5 NOTE: the term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. To avoid any confusion or misunderstanding of the difference between the terms "serious" and "severe", the following clarification should be noted. The term "severe" is not synonymous with "serious". Severity is used to describe the intensity of a specific event (i.e., mild, moderate or severe). The event itself may be of relatively minor medical significance (such as severe headache). Seriousness (not severity), which is based on patient/event outcome or action criteria, serves as a guide for defining regulatory reporting obligations.
SIDE EFFECT	Any unintended effect of a medicinal product occurring at doses normally used in a person, which is related to the pharmacological properties of the drug.
SIGNAL	Information that arises from one or multiple sources (including observations and experiments), which suggests a new potentially causal association or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial6.

5 ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting

6 Cioms.ch. Published 2021. Accessed May 4, 2021. https://cioms.ch/wpcontent/uploads/2021/03/PVGlossary-450x675-1.jpg

UNEXPECTED ADVERSE REACTION	An adverse reaction, the nature or severity of which is not consistent with the applicable product information or characteristics of the drug.

CHAPTER 1: Introduction

1.1 Background

The World Health Organization (WHO) has defined pharmacovigilance (PV) as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other possible drug-related problems." The main aim of a PV system is to protect the public from medicines-related harm.

Medicines-related problems can be the result of several different types of challenges including but not limited to adverse drug reactions, medication errors, therapeutic ineffectiveness, drug-drug and drug-food interactions, quality related issues, etc. In addition to these issues, the increasing availability of new or re-purposed medicines and the need for safety data that can better inform decisions in treatment guidelines have highlighted the need for a strong PV system.

PV systems include all organizations, institutions and resources that contribute to the activities that ensure and promote medicine safety. These activities include the comprehensive identification, management and recording of product-related problems as well as the efficient and timely collection of such problems. It also involves the collation and assessment of reports and the eventual communication of findings elaborating the risks and benefits to support decision-making at various levels of the health care system. The Ministry of Health (MOH) is ultimately responsible for coordinating PV activities and it does so in collaboration with all key stakeholders in both the public and private sectors.

A national PV policy aims at providing broad guidance to all stakeholders following engagement on PV issues with a view of arriving at a logical consensus and commitment to ensure patient safety that is in line with other national policies, strategic plans and guidelines.

The Eswatini National Pharmacovigilance Policy serves as a document to guide PV activities in the country. It also serves as a tool for advocacy geared to provide an enabling environment as well as for effective planning, implementation,

monitoring and evaluation of the PV system by all key stakeholders. The document addresses issues related to the systems and structures required for pre- and post-authorization and the monitoring of safety and effectiveness of medicinal products in the Kingdom of Eswatini.

1.2 Situational Analysis

The Kingdom of Eswatini is a land-locked country of 17,363 km² in southern Africa, neighbouring South Africa on the north, west and south, and Mozambique on the east. In 2017, it had 1,467,152 inhabitants.

The country's health care system consists of a formal and informal sector. In the formal health sector, there are both public and private health service providers, including public health facilities (45%), private facilities (23%), faith-based organizations (15%), industry-owned facilities (12%) and NGOs (5%). In the public sector, there are five (5) levels at which health services are delivered: national referral hospitals, regional hospitals, primary health care facilities including health centres, public health units and outreach sites, and lastly community-based care provided by volunteers.

In Eswatini, Central Medical Stores (CMS) manages the public sector pharmaceutical supply chain system. This department supports the mission of the MOH by providing preventative, curative and diagnostic products that are of acceptable quality, safe and effective. The main objective of CMS is to ensure a regular uninterrupted equitable supply of quality medicines and medical supplies to health facilities in the public sector, thus ensuring that the general Swazi population can access these commodities. The liability of medicinal products supplied through CMS or donors rests with manufacturers and Marketing Authorization Holders (MAHs) of that specific product. Some private health facilities get some TB and HIV medicines, family planning commodities and vaccines from CMS; other commodities are mainly supplied by private pharmaceutical companies that import products into the country. There is currently no pharmaceutical manufacturing in Eswatini.

The Kingdom of Eswatini initiated systematic PV reporting in 2009 by establishing a National PV Unit, which is now called the National Pharmacovigilance Centre

(NPC). A pharmacist at CMS was designated a focal person for these activities. The NPC coordinates all PV activities in the country. These activities have evolved from spontaneous reporting to encompass active surveillance systems initiated in 2015 for patients receiving TB and/or HIV medicines in sentinel sites. The two official adverse event-reporting forms include a spontaneous reporting form and an active reporting form for TB drugs or antiretroviral treatment (ART). Spontaneous reporting forms are available to all health facilities that request them, while active PV forms are only available at 13 MDR-TB sites and an additional three (3) high volume sites that provide HIV treatment services.

The Eswatini National PV Centre has been a member of the WHO Programme for International Drug Monitoring since 2015. The NPC performs direct entry of PV data into its national database VigiFlow®, which is the web-based individual case safety report (ICSR) management system that is available for use by National Pharmacovigilance Centres of the WHO Programme for International Drug Monitoring. It supports the collection, processing and sharing of data of ICSRs to facilitate effective data analysis. This was encouraged in order to ensure proper coding of ADRs and medicines into internationally accepted standard dictionaries, such as MedDRA and WHO-DD, which are built into the software. At the end of April 2020, the number of ICSRs in Vigibase® were 345 cases.

A National Patient Safety Monitoring Committee (NPSMC) was established in 2015 to provide advice to the NPC on PV activities and issues related to the effectiveness of medicinal products. The NPSMC is composed of 16 members who represent different organizations within the country. The NPSMC is chaired by the Deputy Director of Pharmaceutical Services and the NPC acts as Secretariat. The National Tuberculosis Control Programme (NTCP), Eswatini National AIDS Programme (ENAP), National Malaria Control Program (NMCP), and the Expanded Program on Immunisation (EPI) are also represented on this Committee. There is also representation from implementing partners, facilities and the WHO. The Committee aims to provide technical assistance to the NPC on data analysis and validation including causality assessment, risk assessment, risk management, case investigation and, where necessary, crisis management, including crisis communication.

Since the Medicines Regulatory Authority (MRA) with a PV centre has not been formally established, there is no clear mandate for the NPC nor a structure. The NPC is currently housed within the Medicines Regulatory Unit (MRU). The MRU is the unit presently tasked with implementing some medicines regulatory functions in the country. The MRU is reporting to the Office of Deputy Director Pharmaceutical Services. Once formally established, the MRA shall be autonomous, as provided for by the Medicines and Related Substances Control Act of 2016, and it will be able to discharge its day-to-day functions as an independent state-owned institution. The Board of the MRA shall report to the Minister of Health. The PV Centre shall be incorporated within the MRA.

Suppliers of medicines import medicines into the country from international manufacturers. The country is currently not actively registering medicines; consequently, medicines which are registered elsewhere are imported into the country for use. There are therefore no provisions in place for requesting these suppliers to submit PV plans, Periodic Safety Update Reports (PSURs), report adverse drug reactions/medicine safety related issues, etc. The suppliers of medicines are registered by the Ministry as importers of the medicines and are provided with an import certificate. The Ministry also lists the products they import, but these products are not considered as being registered.

In Eswatini, documents which include the National Health Policy, National Pharmaceutical Policy and Medicines and Related Substances Control Act, as well as program guidelines provide limited guidance on PV. There is, however, a strong political will to support PV activities.

Feedback mechanisms and dissemination platforms include: a PV newsletter, titled 'Eswatini Medicine Safety Watch' every quarter, training forums of health care workers (HCW) and data review meetings.

1.3 Policy Development Process

The NPC developed a concept note for the attention of the MOH Senior Management Team (SMT) to advocate for a standalone PV policy. The concept note explained the

importance and advantages of having a standalone policy. After the approval by the SMT to develop the policy, a technical writing team composed of seven (7) local members guided by the Lead for the Policy, Law and Regulations Work Package in the Pharmacovigilance for Africa (PAVIA) project was formed to prepare a zero draft. The zero draft was presented to the Policy and Program Coordinating Unit (PPCU) for review and input. Initial comments from the PAVIA work package II leader and input from the PPCU were incorporated into the zero draft to produce a first draft. The document was then shared with key PV stakeholders, following which a meeting with these stakeholders was organized. In this meeting the stakeholders were able to provide input and discuss the document. The contributions from PV stakeholders were incorporated to develop a second draft. The second draft document was presented to the MOH SMT for their consideration. Comments and input from the MOH SMT were incorporated resulting in final draft of the document, which was subsequently endorsed by the Minister of Health.

1.4 Rationale and Scope of the Policy

1.4.1 Rationale

The safety of medicinal products may be impacted by a diverse array of factors, which include the pharmacological properties of the product, the genetic disposition and culture of patient, treatment-seeking behaviour of patients (including extensive self-medication, unbridled access to prescription-only medicines, misuse of antibiotics and preference for injection), disease pattern and comorbidities. Other factors include product quality, due to among other things the drug manufacturing processes, distribution and storage conditions. Further, substandard and counterfeit medicines, medicine use practices and indiscriminate use of traditional, complementary and alternative medicines may also play a role.

Generally, the safety of a medicine is studied at most amongst a few thousand patients pre-registration. As a result, only the early onset and most frequent adverse reactions are likely to surface by the time the product is registered for marketing. Important adverse reactions may not be known at the time of registration and can only be discovered after the medicine is in use by a larger population of patients.

PV data generated in Eswatini shall not only have greater clinical and educational significance, but it will also assist the institution responsible for medicinal product regulation and public health programmes to make evidence-based product decisions as the information obtained in one country (e.g., the country of origin of the medicinal product) may not be relevant to other parts of the world, including Eswatini, where demographics, disease profiles and medical practices differ. PV helps ensure that patients obtain safe and effective medicines and other pharmaceutical products.

The post-market surveillance of adverse drug reactions (PV) is therefore clearly an important element of the regulation of medicines that should be instituted in all countries, including in Eswatini.

1.4.2 Scope of PV Policy

This policy shall guide and provide an enabling environment for effective planning, implementation, monitoring and evaluation of the PV system in the country for government, private, not for profit, private for-profit health sectors, non-governmental organizations and implementing partners involved in health service delivery in the Kingdom of Eswatini.
The Eswatini Pharmacovigilance Policy covers safety monitoring of the following: medicines, vaccines, blood and blood products, biologicals, herbal medicines, traditional and alternative remedies including food supplements and oils used in Eswatini.

This monitoring system shall lead to early detection of adverse drug reactions, interactions and other medicine-induced problems as well as the detection of previously unknown adverse reactions (signals). It also facilitates the identification of suspected product quality problems, therapeutic ineffectiveness, medication errors and predisposing risk factors. Furthermore, it can help in identifying the possible mechanisms underlying adverse reactions and shall ensure communication throughout the life cycle of the medicine.

The policy shall also be a guiding document for the establishment of national PV systems for the reporting of adverse events to national and, if appropriate, regional PV centres and global databases.

This policy shall also not only provide guidance on the mechanisms that shall be used to strengthen reporting of adverse events, but it shall also guide how the reporting of periodic safety updates by manufactures and importers for the products they place on the market can be incorporated into the national PV system. PV regulation and guidelines shall delineate the implementation of this policy. This policy shall also articulate the critical role of NPC in clinical trial oversight.

1.5 Analysis of National PV Centre related Strengths, Weaknesses, Opportunities and Threats

Strength

1. Existence of National Pharmacovigilance Centre with designated PV personnel
2. The political goodwill of government to support the growth of PV
3. The existent Medicines and Related Substances Control Act No. 9 of 2016 provides a potential enabling environment and a substrate for various facets of PV to build on
4. The commitment of various health programmes to incorporate PV into their activities

Weaknesses

1. Limited personnel disposition in numbers and expertise at NPC and around the country to deal with PV
2. The lack of resources (human, financial and infrastructure) to facilitate the growth of PV
3. The lack of training resources and platforms for PV locally
4. The country also lacks basic infrastructure to undertake PV activities
5. Inconsistent PV reporting
6. Limited/delayed feedback on PV data
7. No reports from medicine manufacturers and importers

Opportunity

1. Technical and financial support donors and partners
2. Collaboration with public health programmes and departments within the Ministry

Threat

1. Fiscal challenges
2. Reliance on donor funding for PV activities

CHAPTER 2: Policy Attributes

2.1 Vision Statement

To establish a PV system that safeguards the health of the population of Eswatini by ensuring that the benefits of medicinal products outweigh the risks associated with their use.

2.2 Mission Statement

To set up an efficient PV system for the early detection of adverse reactions and other related problems associated with medicinal products, receive and promptly process reports from the public, suppliers of medicines, healthcare professionals and consumers that are safety-conscious and to respond appropriately to prevent or limit medicinal product-induced harm.

2.3 Goal and Objectives of the National Pharmacovigilance Policy

2.3.1 Goal

The goal of the National Pharmacovigilance Policy is to provide a strategic framework for the integration of PV into the healthcare system of the Kingdom of Eswatini, thereby ensuring overall safety in the use of medicinal products.

2.3.2 Objectives

The objectives of the National Pharmacovigilance Policy are:

- To comprehensively address a system for the safety monitoring of adverse events/reactions to medicinal products.
- To specify the roles and responsibilities of all stakeholders in PV in the Kingdom of Eswatini.
- To serve as a tool to solicit for political support and commitment, as well as highlight the need of an independent, sustainable sources of funding for the operation of an effective pharmacovigilance system.
- To integrate PV into the healthcare system, including all public health programmes, and to ensure the rational and cost-effective use of medicines

and other products.

- To provide a framework for research in PV.
- To provide a basis for future legislation in PV, including the reporting of adverse events within the health care system by all stakeholders.

2.4 Scope of the National Pharmacovigilance Policy

The National Pharmacovigilance Policy shall cover pre- and post-approval safety monitoring of medicinal products in the country. This policy shall serve as a tool for providing an enabling environment for effective planning, implementation, monitoring and evaluation of the PV system at all levels of health service system including partners, private health sectors and public health programmes.

The policy shall provide guidance to both public and private health facilities, importers/MAH and clinical trials to detect, manage, report and communicate adverse drug reactions. This document shall similarly guide the National Pharmacovigilance Centre in the coordination of PV activities in the country and implementation this policy framework.

2.5 Guiding Philosophy and Principles

The policy shall be based on the following guiding principles:

a) Good quality healthcare is assured through application of PV principles and practice in private and public healthcare systems at all levels in order to ensure patient safety.
b) Patients' access to safe and rational use of medicinal products and vaccines.
c) Healthcare professionals are to consider PV practice as a professional responsibility.
d) Integration of PV into the overall health system both public and private.
e) Existence of consistent and effective partnerships and collaboration with all stakeholders.
f) Existence of financial commitment to all levels of the healthcare system for sustained safety monitoring of medicines and other medicine-related issues.

CHAPTER 3: Policy Directives

This section of the policy document outlines the elements of policy directives that are related to the PV system and regulatory framework for PV. This chapter includes the Pharmacovigilance Policy declarations and commitments; an outline of the comprehensive PV system envisioned for Eswatini; the PV methods to be implemented in the country, the regulatory framework and data privacy for PV adopted.

3.1 Pharmacovigilance Policy Declaration and Commitment

The National Pharmacovigilance Policy shall be guided by the following declarations and commitments:

a) The government and all stakeholders in the public and private sectors of the health system shall commit themselves to all actions necessary to achieve the goal and objectives of the policy.
b) The government and the private sector shall commit to PV as a vital component of quality healthcare delivery and shall deploy resources to the implementation of PV and related activities.
c) The National Pharmacovigilance Centre shall be committed to providing timely and reliable information to consumers, health care professionals and stakeholders.
d) All healthcare professionals are convinced that detecting and reporting of ADRs and other medicine-related problems is not only their professional responsibility but also contributes to better healthcare delivery and improves quality of life.
e) Development partners shall participate actively and collectively in promoting PV activities and resource mobilization.
f) There shall be one national PV system in Eswatini coordinated by the NPC.

3.2 Pharmacovigilance System

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems. Recently, its concerns have been widened to include herbals, traditional

and complementary medicines, blood products, biological, medical devices and vaccines. Many other issues are also of relevance to the science; these include:

a. Substandard and falsified medicines
b. Medication errors
c. Lack of effectiveness reports
d. Abuse and misuse of medicines
e. Adverse interactions of medicines with chemicals, other medicines and food

The information collected during the pre-marketing phase of a medicine is inevitably incomplete with regard to possible adverse reactions because: tests in animals are insufficiently predictive of human safety, in clinical trials, patients are selected and limited in number, the conditions of use differ from those in clinical practice and the duration of trials is limited. In addition to this, information about rare but serious adverse events, e.g., chronic toxicity, use in special groups (such as children, the elderly or pregnant women) or medicine interactions is often incomplete or not available. In addition, there are new kinds of safety concerns such as:

- Illegal sale of medicines and drugs
- Increasing self-medication practices
- Irrational and potentially unsafe donation practices of medicines and related products
- Widespread manufacture and sale of counterfeit and substandard medicines
- Increasing use of traditional medicines outside the confines of the traditional culture of use
- Increasing use of traditional medicines and herbal medicines with other medicines with potential for adverse interactions
- Usage of repurposed medicines

A PV system is needed for the prevention of medicine-induced and product-related human suffering that arises because of adverse drug reaction, medication errors (errors in prescribing, transcribing, dispensing and administration), poor product quality and to avoid financial risks associated with unexpected adverse effects.

Eswatini shall establish a comprehensive PV system at the national and health facility level that will monitor all medicine-related harm in addition to the monitoring

of known and unknown adverse drug reactions. This medicine-related harm shall include medication errors (prescribing errors, transcribing errors, dispensing errors and administration errors), therapeutic ineffectiveness (which may result from medicine interactions, antimicrobial resistance, etc.) and product quality problems. Collecting medicine safety data from health professionals using the spontaneous reporting system only is not sufficient. The system shall therefore also expand towards employing more active surveillance methods, in specific instances and for limited periods through the search for exposures or events using disease/medicine registries, sentinel sites and cohort event monitoring.

As described in Figure 1, the framework of a comprehensive PV system has three (3) main components in the monitoring of medicines safety. These are the people, the functions and the structures that are necessary in the collection of the inputs, the process of analyzing such inputs and the final output that is used for decision-making and necessary actions.

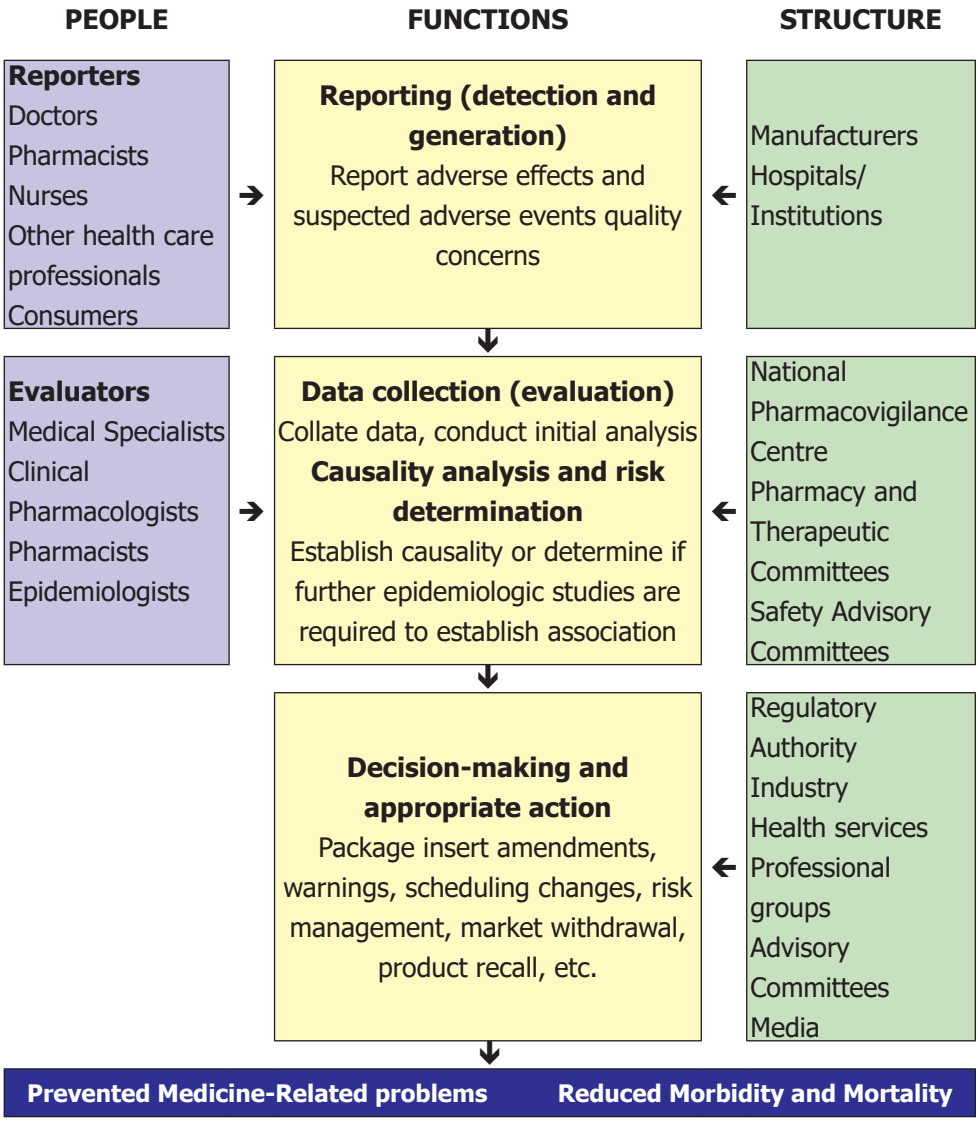

Figure 1: The Pharmacovigilance Framework: relating people, functions structures and expected outcome and impact. (Strengthening Pharmaceutical Systems (SPS). Supporting Agency for international development by the SPS Program. Arlington, VA: Management Sciences for health). Pharmacovigilance in developing countries: The systems perspective. Submitted to the U.S.

Table 1:The input–process–output (IPO) framework of the Policy

Input	The function of detecting and reporting medicines safety information obtained from the reporters (suppliers of products, all health care professionals, consumers) voluntarily or mandatorily.
Process	The collection, collation, assessment and analysis of medicines safety data to determine the adverse events severity, causality and preventability through the support of evaluators at the Pharmacy and Therapeutics Committees (PTCs) at facility level, expert committees and by the National Patient Safety and Monitoring Committee (NPSMC) at the National level.
Output	Decisions and actions made after the analysis; whether its information from the feedback to the reporters; parties receiving the information (industry, health services, professional groups, media); the type of regulatory actions taken nationally (package insert amendments, warnings, scheduling changes, risk management, market withdrawal, product recall, access/distribution control, procurement programme etc.) and at facility-level (individual case management)

3.3 Pharmacovigilance Methods

The Eswatini National Pharmacovigilance Centre (NPC) shall use any of the methods of PV mentioned below to collect safety information from different sources. In all, the NPC shall decide, in collaboration with public health programmes and health facilities, the scope and mechanisms of facilitating the PV methods through PV guidelines, SOPs and job aids.

3.3.1 Passive Pharmacovigilance Method

Passive PV system means that no active measures are taken to look for adverse effects other than the encouragement of health professionals and others to routinely monitor and report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common PV method. In some countries this form of reporting is mandatory.

Spontaneous reporting of adverse events identified during the use of any medicinal product is mandatory for the manufacturer/importer or marketing authorization holder (MAH) of that product. It shall also be mandatory to report serious adverse events occurring during clinical trials conducted in Eswatini. Spontaneous reporting of adverse events suspected to be related to the use of a medicinal product is an ethical responsibility for all healthcare professionals. No claims of medical malpractice can be based solely on a submitted report. Reports received by the Centre as part of spontaneous reporting shall not be made available to support any legal, administrative or any other action that may be detrimental to the reporting health professional or the patient.

Methods like spontaneous reporting, and targeted spontaneous reporting shall be used in the country.

3.3.2 Active Pharmacovigilance Method

In contrast to spontaneous reporting, active reporting seeks to ascertain completely the number of adverse events via a continuous pre-organised process. The NPC shall undertake active methods of PV either solely or in collaboration with relevant stakeholders. The methods of an active PV system like reviewing patient files/ interviewing patients at selected sentinel sites, Cohort Event Monitoring system (CEM), registries or active Drug Safety and Monitoring system (aDSM) shall be implemented in the country. The NPC shall also put in place a process for the detection of signals of public health importance that require further evaluation through active surveillance. Further guidance on the implementation of the methods shall be provided on the National PV guideline and SOPs.

3.3.3 Comparative Observational Studies

Comparative observational studies are epidemiologic methods that are a key component in the evaluation of adverse events. Major types of these designs include cross-sectional studies, case-control studies and cohort studies (both retrospective and prospective).

The NPC shall introduce this method of PV system whenever necessary either solely or in collaboration with researchers/ PV stakeholders.

3.3.4 Drug Utilization Studies

Drug utilization studies (DUS) describe how a medicine is marketed, prescribed and used in a population, and how these factors influence outcomes, including clinical, social, and economic outcomes. These studies provide data on specific populations, such as the elderly, children or patients with hepatic or renal dysfunction, often stratified by age, gender, concomitant medication and other characteristics.
The NPC shall work with different organizations, institutions, and individuals to coordinate the DUS when needed.

3.3.5 Reporting of Medication Errors

The generation of information on medication errors and its dissemination minimizes similar occurrences in clinical practice.

To achieve this goal the NPC shall:	
a.	Ensure that healthcare professionals report any case of medication error
b.	Maintain a database for medication errors
c.	Carry out an appropriate root cause analysis on the reported medication errors
d.	Disseminate information on medication errors to prevent future occurrence

3.3.6 Reporting of Suspected Cases of Substandard and Falsified Medicines and Other Related Products

Recognizing the menace of substandard and falsified regulated products, PV shall be used as an additional vital tool towards checking the trend. Existing PV processes shall be strengthened for detecting substandard and falsified medicines. Suspected lack of effectiveness observed by healthcare professionals and consumers of any medicine and other related products shall be reported to NPC.

3.4 Regulatory Framework for Pharmacovigilance

3.4.1 Mandatory or Voluntary Reporting

PV reporting and the submission of periodic safety updates by manufacturers, MAHs and importers who place products on the market in Eswatini shall be mandatory. All these manufacturers, MAHs or importers are to report to the NPC, any adverse events associated with their products that come to their attention in Eswatini or anywhere in the world.

Healthcare professionals should note that the reporting of ADRs and other medicine-related problems is a professional and ethical responsibility, which enhances the quality of healthcare given to the patient.

The reporting of ADRs and other medicine-related problems shall apply as follows:

a) It shall be an ethical responsibility for health professionals.
b) There shall be no remuneration for reporting of ADRs.

3.4.2 Sources of Reports/Who Should Report

Sources of reports shall include:

Individuals

Doctors, pharmacists, nurses, complimentary medicine professionals or other healthcare professional in the public or private sector who, on their own initiative, send reports of adverse drug reactions and other medicine-related problems to NPC.

Institutions

Healthcare institutions, including hospitals, NGOs, Mission facilities, clinics, medical centres, research institutes and Public Health Programmes operating in the public or private sectors.

Complimentary

Herbal medicine institutions/centres/associations.

Manufacturers

Importers/distributors of products covered by this policy, retailers, MAHs, complimentary and other related products.

Patients

Consumers report through their healthcare professionals who will in turn forward the report to NPC or where this impossible direct report to NPC can be made.

Other Relevant Resources

Scientific literature, legal documents.

3.4.3 What is to be Reported?

a. All adverse events due to all medicinal products covered under the scope of PV.
b. All medicinal product-related problems such as medication errors, lack of effect, drug interactions, etc. shall also be reported.
c. Clinical trials shall be operated with Drug Safety Monitoring Boards for reporting and documenting adverse events.

3.4.4 How to Report?

All suspected ADRs and medicinal product-related problems shall be reported to NPC using appropriate reporting tools. The Centre uses spontaneous ADR reporting forms and active ADR reporting forms that will assist in collecting passive and active PV data respectively.

3.5 Data Privacy

Unique identifiable information and sensitive personal data of a patient, consumer and/ or the reporter of an adverse event shall remain highly confidential. All personal data received by NPC is processed exclusively for PV purposes.

3.5.1 Personal Data Collected for Pharmacovigilance Purposes

The NPC, Health care facilities and MAHs may collect personal data directly from the patient/consumer, or from anyone reporting the patient/consumer's symptoms on their behalf. The personal data include but are not limited to the following:

d. Patient's initials, contact details, email, telephone number, address, date of birth, gender, weight, height and related demographic data.
e. Medicines and products taken including dosages, medical history, adverse events/reactions and laboratory reports.
f. Reporter's name, contact details, including email, telephone number, address, professional role and patient relationship.
g. Special Category Data: This includes any information that tells us about a patient's – health, racial/ethnic origin, genetic data and sexual orientation.

3.5.2 Use of Personal Data for Pharmacovigilance Purposes

In order to meet international reporting obligations, anonymized personal data may be used and shared to:

a. Investigate the adverse event.
b. Contact patient/consumer/reporter for further information about the adverse event reported.
c. Collate and analyse the information about the adverse event.

3.5.3 Sharing/Disclosure of Personal Data for Pharmacovigilance Purposes

Personal data collected from the patient, consumer and/or reporter in accordance with this Policy shall strictly be kept confidential. However, specific data may also be transferred to a third party in the event of storage and analysis. Certain anonymized personal data may be shared with Uppsala Monitoring Centre (UMC) or to other third parties with approval.

NPC, institutions, research entities and/or individuals may publish information about adverse events (such as case studies and summaries) on approval from the Eswatini Health and Human Research Review Board (EHHRRB). NPC will ensure personally identifiable data is not included in any publications so that no individual can be uniquely identified.

3.5.4 Statement of Policy on Data Ownership

Data collected by the NPC shall belong to the Kingdom of Eswatini Ministry of Health. The MoH reserves the right to review and approve of all public health data before it is released to the public or any other third party.

The Ministry of Health, through NPC, will provide appropriate administrative, technical and physical safeguards to ensure the confidentiality and security of the data and to prevent its unauthorized use or access. Except as authorised in writing, the MOH shall not disclose, release, reveal, show, sell or otherwise grant access to the PV data.

3.5.5 Statement of Policy on Data Sharing

NPC shall share anonymised PV data with the stakeholders upon formal request from the Centre. Organizations, individuals or any government entities shall request for data from the Centre based on the following data sharing terms and conditions set under this section of the policy. In addition to the following requirements, NPC shall request for additional information where necessary.

Table 2: Terms and Conditions for Data Sharing

Type of Stakeholder	Specific data need	Permission requests required
Public Health Programmes	• Summarized data with no personal identification information	• Email request
	• ICSRs for the purposes of programmatic usage • Signal detection and causality assessment exercises	• Formal letter addressed to the MRU focal person or Head of MRA once established and NPC focal person • Data collection tool or data
	• ICSRS for the purposes of publication and other means of dissemination	• Ethical clearance should be obtained from EHHRRB
UN Agencies and Partners	• Summarized data with no personal identification information	• Data sharing agreement should be signed by MOH • The agency/organization should attach the dataset
	• ICSRs for different purposes other than dissemination	• Data sharing agreement should be signed by MOH • The agency/organization should attach the dataset
	• Signal detection and causality assessment exercises	• Ethical clearance should be obtained from EHHRRB • Data sharing agreement should be signed by MOH
Individuals/ Researchers/ Universities	• PV data for research purposes and publication	• Ethical clearance should be obtained from EHHRRB

3.5.6 Security of Personal Data

The NPC shall take measures to secure personal data from accidental loss and from unauthorised access, use, alteration or disclosure. Additionally, NPC will take further information security measures including access controls, stringent physical security and robust information collection, storage and processing practices for ensuring security of personal data.

CHAPTER 4: Policy Directives

This section of the policy document outlines the elements of policy directives that are related to the country's PV system structure, functions and stakeholders' responsibility.

4.1 Pharmacovigilance Structure and Functions, Roles and Responsibilities of Stakeholders

4.1.1 The Structure of Eswatini Pharmacovigilance System

The structure of the PV system in Eswatini shall be as follows:

1. The National Pharmacovigilance Centre (NPC), located at the Medicine Regulatory Unit (MRU) or the Medicines Regulatory Authority once established, is responsible for the overall management of the PV system.
2. PV systems will be integrated into public health programmes including the Expanded Programme on Immunization (EPI).
3. Pharmaceutical establishments operated by pharmaceutical industries and importers shall submit reports to the NPC.
4. Both public and private health facilities shall submit reports to the NPC.
5. The National Patient Safety and Monitoring Committee (NPSMC) shall analyse and disseminate the information (establishment / line of authority).

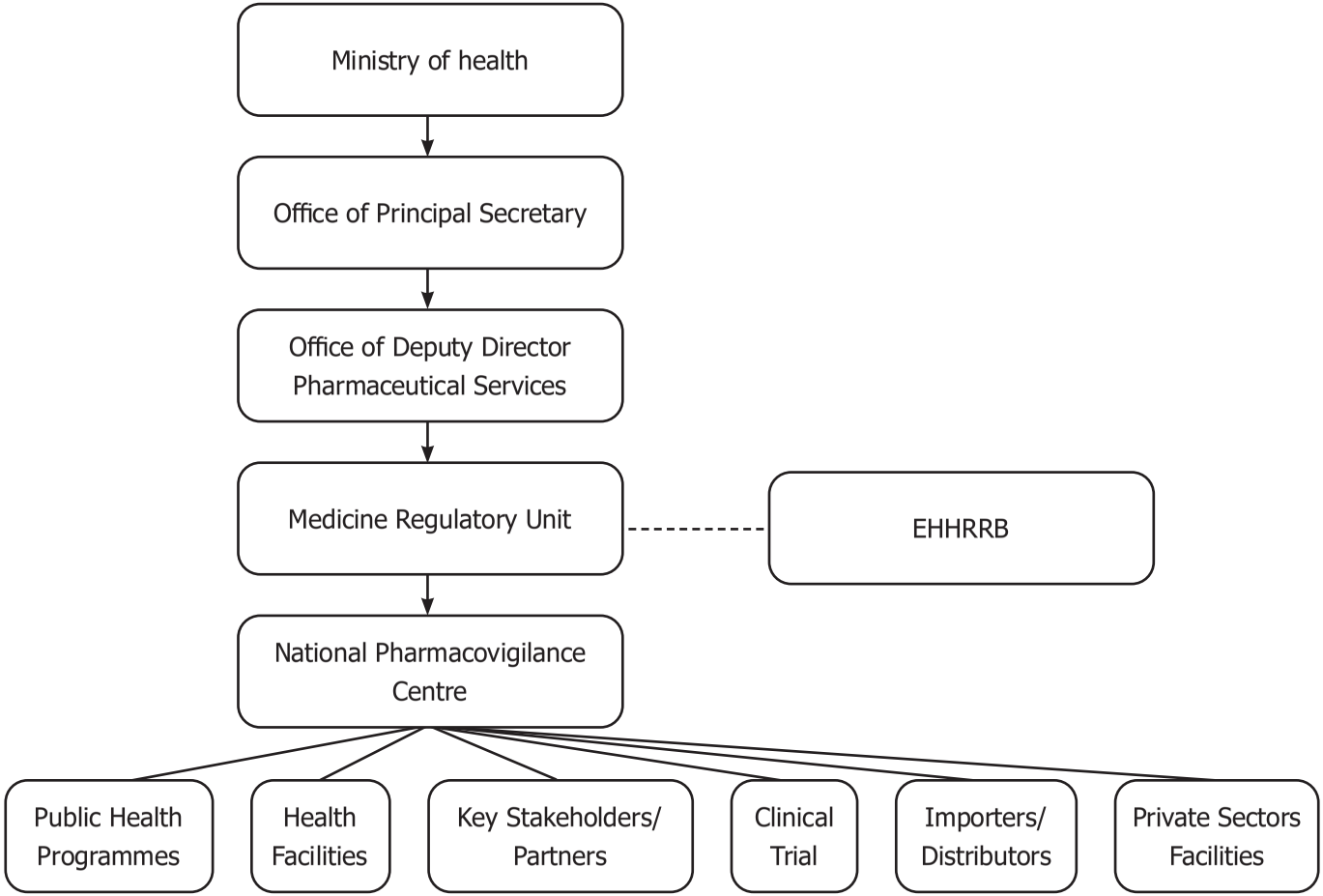

Figure 2: Structure of Eswatini Pharmacovigilance System

4.1.2 Role and responsibilities of MOH

The Ministry of Health shall:

a. Appoint members of NPSMC on recommendation of the Principal Secretary. Such appointment would be the responsibility of the MRA board once the MRA is established.
b. Make available comprehensive policy guidance on PV activities.
c. Advocate for sufficient funding of PV activities at all levels of healthcare delivery.
d. Provide political support for the establishment and sustainment of PV in healthcare institutions across the country.
e. Monitor and evaluate the PV programmes for compliance with the objectives of the policy.

4.1.3 Role and Responsibilities of the National Pharmacovigilance Centre (NPC)

The National Pharmacovigilance Centre shall be under Medicine Regulatory Unit and shall report directly to MRU. It shall be the operational hub of PV activities. The National Pharmacovigilance Centre shall:

a. Be responsible for the day-to-day running of the national PV system and shall undertake all necessary actions and activities to ensure safe and effective medicines for Eswatini.
b. Collect and manage adverse drug reaction (ADR) reports as well as reports of medication errors and suspected substandard and falsified medicines.
c. Develop and distribute various tools and reporting forms for reporting ADRs, medication errors, product quality defects and other medicine-related problems.
d. Prepare PV guidelines, standard operating procedures, tools (including reporting forms) and job aids for PV.
e. Collaborate with all public health programmes for the distribution, collection and collation of reports of adverse events.
f. Be responsible for managing all reports received including providing

feedback to reporters, collation of reports and submission of reports to the WHO global ICSR database.

g. Provide secretariat function to the NPSMC and collaborate with the members for the generation of signals and the analysis of PV information.
h. Identify signals of drug safety, i.e., unknown or poorly characterized adverse events in relation to a drug or drug combination and/or its use.
i. Educate healthcare professionals in public health programmes to recognize PV practice as professional responsibility and be more committed to it.
j. Undertake assessment of risks and options for risk management.
k. In collaboration with the MRU inspectorate, periodically conduct PV inspections of pharmaceutical industries to verify compliance with regulations, monitor routine activities in the industry every year or if required to investigate a problem.
l. The Centre shall be responsible to collate, analyse and disseminate patient safety information on different platforms including, but not limited to, newsletters, reports, and presentations on different national, regional and international platforms, including but not limited to peer-reviewed journals.
m. Contribute to the design and approval of clinical trials evaluating medications not yet approved by the appropriate regulatory bodies.
n. Collaborate with academic institutions in ensuring that PV is incorporated into the curriculum of pharmacy schools.

4.1.4 Functions of the National Patient Safety and Monitoring Committee (NPSMC)

The National Patient Safety and Monitoring Committee (NPSMC) is made up of various experts/specialists in such fields as clinical medicine, pharmacy, drug regulation, epidemiology, health programmes and partners. The Deputy Director of Pharmaceutical Services (DDPS) shall serve as the Chairperson of the Committee. The Committee shall have the following functions:

a. To assist the NPC to foster a culture of PV reporting in Eswatini.
b. To promote optimal safety of medicines and related products used in Eswatini.

c. To support the regular review of data analysis findings and validate findings before stakeholder dissemination by the NPC.
d. To recommend possible regulatory measures based on PV data received from various facilities.
e. To assist the NPC in taking appropriate decisions towards medicines and related products used in Eswatini.
f. To develop a clear communication strategy for routine communication and crises communication.
g. Assist the NPC to:
    - Monitor medicines as used in everyday practice to identify previously unrecognised adverse effects or changes in the patterns of their adverse effects.
    - Assess the risks and benefits of medicines to determine what action, if any, is necessary to improve their safe use.
    - Provide information to users to optimise safe and effective use of medicines.
    - Monitor the impact of any action taken.

4.1.5 Roles and Responsibilities of Manufactures/Importers/Marketing Authorization Holders

Manufacturers and importers of medicinal products covered by this policy shall:

a. Establish a PV system headed by a Qualified Person for Pharmacovigilance (QPPV) to handle all medicine-related problems. The QPPV should be placed in Eswatini and should be qualified, with documented experiences and training in all aspects of PV.
b. Have PV system master files (PSMF).
c. Report any serious ADR during clinical trials as required by existent guidelines.
d. Conduct post-marketing surveillance on its own on products they market as deemed relevant or as may be requested by the regulatory authority.
e. Promptly forward periodic safety update reports (PSURs) to the NPC (biannually for two years (2) for new products, annually for a further two (2) years and thereafter every five (5) years) as well as the Periodic Benefit

Risk Evaluation Report (PBRER) as stipulated in the existent guidelines.

f. Provide adequate information to consumers on the products they market.
g. Collaborate with the NPC on safety issues concerning the products they market.
h. Report any serious international incidents relating to their products. The period for reporting Serious AEs shall be 15 calendar days from the time a drug company receives notification (referred to as "Day 0") of such a case.

4.1.6 Roles and Responsibilities of the QPPV

The Qualified Person Responsible for Pharmacovigilance (QPPV) is an individual who is responsible for the safety of the human pharmaceutical products and shall be responsible for the following:

a. Establish (if absent) and manage the PV system of the industry/MAH.
b. Develop and/or maintain the Pharmacovigilance System Masterfile (PSMF).
c. Oversee the handling of all case reports ensuring appropriate handling of the expedited reports (7-days to 15-days) with appropriate content in a timely manner as well as address aggregate reports e.g., PSURs and PBRERs.
d. Evaluate the PV system in a sustainable manner during the post-authorization period.
e. Oversee the various PV activities including, but not limited to, signal detection and management, risk management, post authorization safety studies (PASS) and risk minimization.
f. Monitor information regarding the benefit-risk assessments of all registered medicines that they are marketing.
g. Provide any safety information and address any request from the authority in a prompt and timely manner.

4.1.7 Roles and Responsibilities of Healthcare Professionals

Healthcare professionals include medical doctors, pharmacists, dentists, nurses, midwives, medical laboratory scientists, etc. All healthcare professionals, irrespective of their specialisation, shall be considered key stakeholders in the PV system. They shall:

a. Detect and manage ADR and other medicine-related problems.
b. Report ADRs and other medicine-related problems occurring in patients/consumers.
c. Conduct appropriate analysis of data including causality assessment and usage.
d. Educate patients on rational use of medicines.
e. Educate and counsel patients on the need to report ADRs and other medicine-related problems when they occur.
f. Educate fellow healthcare professionals on PV.

4.1.8 Roles and Responsibilities of Health Facilities

All health facilities in which medicinal products covered by this policy are used shall be involved in PV activities. Specific roles shall include the following:

a. Setting up of PV Committees (PV sub-committee under PTC, where PTC is present) on safety of medicinal products.
b. Ensure the generation of ADR reports.
c. Educate and counsel patients and clients about safety issues associated with medicinal products.
d. Train personnel on PV and create an enabling environment for participation in PV programmes.
e. Assisting signal detection and investigations.
f. Facilitate communication with NPC and other structures that are part of the PV system in the country.

4.1.9 Roles and Responsibilities of Health Professional Associations

Healthcare professional associations shall:

a. Participate in activities that strengthen the PV system in the country.
b. Encourage their members to take active part in PV.
c. Provide incentives like continuous professional development credits to encourage their members to participate in PV.
d. Be responsible for PV education, promotion and advocacy.

4.1.10 Roles and Responsibilities of Public Health Programmes (PHPs)

Public health programmes including the Expanded Programme on Immunization (EPI), shall consider PV and safety monitoring as an essential, critical and indispensable part of their activities.

Together with the Pharmacovigilance Centre, the PHPs shall:

a. Deploy responsive PV systems and activities to ensure the protection of patients and the public, as well as to promote the safe and cost-effective use of medicines, vaccines and health commodities.
b. Collaborate with the NPC to develop programme-specific guidelines on effective communication and shall develop crisis management plans for their programmes.
c. Participate in PV research.
d. Undertake all other activities to ensure patient safety within the programmes.
e. Support the funding of PV activities.

4.1.11 Roles and Responsibilities of Donors and Technical Assistance Partners

Donor agencies and development partners that support the procurement of products shall:

a. Ensure the existence of capacity of the safety monitoring of the procured products.
b. Provide the necessary technical, financial and logistical support to the MOH, health facilities and health professionals.
c. Designate funds for safety monitoring of products and encourage the responsible deployment of products taking into consideration the healthcare system and the availability of health professionals and health facilities.

4.1.12 Role and Responsibilities of Academia

Academia including health professional training institutions like Schools of Medicine, Pharmacy, Nursing and Public Health shall ensure pre-service training through the incorporation of PV into the undergraduate curriculum. The academic institutions shall:

a. Support the National Pharmacovigilance Centre in their area of expertise

including research in PV, publications and the development of tools and methods for PV.

b. Develop PV module and incorporate into regular curriculum of Diploma, undergraduate, post-graduate courses (including Masters and Doctorate programmes).

4.1.13 Roles and Responsibilities of Eswatini Health & Human Research Board and MoH Research Unit

The Eswatini Health and Human Research Review Board (EHHRRB) shall ensure that all clinical trials, study protocols and proposals have integrated active medication safety reporting. Where appropriate, the EHHRRB shall insist that the principal investigator reports all serious adverse events occurring during any study to the NPC regardless of the nature of the study. The reporting requirements for AEs within a clinical trial will also be guided by the Principles of Good Clinical Practice (GCP), national regulatory requirements and the nature of the study.

4.1.14 Role and Responsibilities of Clinical Trial Investigators

Clinical Trial Investigators must report Suspected Unexpected Serious Adverse Reactions (SUSARs) and Unanticipated Serious Adverse Device Effects (USADEs) to NPC within defined timelines:

- Fatal/life-threatening within 7 days
- Non-fatal/life-threatening within 15 days

4.1.15 Role and Responsibilities of the Media

The media shall play an advocacy role for PV in line with the traditions, ethics and principles of the journalism profession. The media shall:

a. Ensure fairness, transparency, balance and equity in its reporting of issues relating to PV and shall avoid sensationalism, trivialisation or the peddling of rumours.

b. Give high priority for patient safety as well as national interest when reporting on PV.

In view of the important and sensitive role of vaccines in public health, the media shall pay particular attention to and exercise extreme due diligence when reporting vaccine safety issues.

4.1.16 Patients, Patient Groups and the Public

Patients, patient groups, associations and the public shall report all suspected adverse reactions to health products. Reports could be sent directly to the NPC or through healthcare professionals at the health facility closest to them.

4.2 Funding of Pharmacovigilance System

The organization and administration of the NPC requires regular source of funds in order to carry out all activities needed for successful and sustained implementation of the system. PV activities shall be funded:

a. By government through appropriate budgetary provisions.
b. Through the fees collected from regulatory activities of the Medicines Regulatory Unit or Medicines Regulatory Authority once established.
c. By key stakeholders with an interest in PV.
d. Institutions such as health insurance companies and health insurance funds, university departments, PHPs, professional associations and governmental departments with an interest in drug safety shall also fund the PV Centre.

In view of the public health consequences of adverse reactions, the continuity of the funding of PV should be guaranteed and not be susceptible to possible pressure groups, political changes or economic factors. MAHs shall not directly fund the NPC.

4.3 Pharmacovigilance Information System

One of the primary responsibilities of the NPC is to make the latest high quality credible medicine and related products information available to health care professionals and key PV stakeholders. For this, the Centre shall have access to up-to-date information including a comprehensive literature database. The Centre

shall preferably have an online access to the UMC database and be on the mailing list of ADR bulletins of WHO.

In order to sustain a successful PV system:

a. The National Pharmacovigilance Centre shall operate a national data bank.
b. Information obtained from ADR reports shall be duly communicated to manufacturers, importers and/or MAHs to effect the appropriate changes (e.g., change in the label, withdrawal, etc.).
c. The information from the data bank shall be shared as necessary with other National Centres and the WHO global drug safety database.
d. Newsletters, medicine bulletins, reports and publications in various pharmaceutical journals may be chosen as routes of effective dissemination of latest developments in medicine research and therapy to the healthcare professionals.
e. Relevant information shall be incorporated into the National Health Management Information System.

4.4 Pharmacovigilance Research and Development

Research and development play a major role in the growth of the discipline. Areas to be addressed by the NPC to ensure the safe use of medicines and related products and limit adverse consequences shall include:

a. Operational research to facilitate ADR-reporting or other medicine related problems, feedback information, dissemination of information and communication to the health professionals and the public.
b. Development of needed competencies for evaluation, causality assessment and validation of case reports, including training of staff in methods of ADR-signal detection and causality assessment.
c. Strengthening the existing PV system to adequately focus on herbal medicines and related products.
d. Use of appropriate PV methods to enable the early evaluation and detection of adverse events during large-scale deployment of medicines and related products in public health programmes.
e. Research collaborations with public health programmes to share and

disseminate the results of such deployments.

f. Building capacity and conducting targeted research in the area of pharmacoepidemiology, pharmacogenomics and drug metabolism as a fundamental tool in active PV.

4.5 Human Resources for Pharmacovigilance

Adequacy of human resource for PV shall be ensured by the recruitment, training and retention of qualified personnel. The Ministry of Health will be responsible to mobilize resources to cover the human resource gap. Once MRA is established HR within the NPC will be the responsibility of the MRA. To ensure the effective implementation of PV activities within the healthcare system, human resources shall be deployed appropriately. Deployment shall entail the engagement of staff to facilitate the various activities as follow:

a. A qualified person with adequate training in PV shall head the NPC. A team of appropriate health professionals and supporting technical and clerical staff shall assist him or her.

b. All personnel involved in PV shall undergo periodic training in order to update their knowledge and increase their capacity to deliver on the job.

CHAPTER 5: Framework for Implementation of the Eswatini National Pharmacovigilance Policy

5.1 Introduction

PV is an important discipline that is growing. Its integration, into the healthcare system should be strengthened to ensure the safe and rational use of medicines and related products. A holistic approach is recommended in the implementation of the National Pharmacovigilance Policy to cover the entire scope of PV and the products in all tiers of the healthcare system. To achieve the policy goal and objectives, the various stakeholders in the healthcare system should be adequately engaged.

5.2 Stakeholders

A crucial initial step in the implementation of the policy is the identification and engagement of all the stakeholders. They should be aware of their roles and responsibilities. Essentially the stakeholders identified include:

a. Ministry of Health
b. Ministry of Education
c. Ministry of Finance
d. Manufacturers/Importers/Marketing Authorization Holders
e. Healthcare professionals including but not limited to Doctors, Pharmacists, Nurses, Laboratory technologists, Pharmacy Technicians, Radiographers
f. Health facilities
g. Health professional associations (Physicians Association, Pharmacists Association, Nurses Association)
h. Public Health Programmes (PHPs)
i. Supporting partners
j. Academia including but not limited to universities and colleges
k. Eswatini Health and Human Research Review Board
l. Patients, Consumers, Patient groups and the Public
m. The media, both electronic and print
n. Professional Regulatory bodies including but not limited to Eswatini Medical and Dental Council, Nursing Council, Eswatini Higher Education Council

o. Regional Regulatory Agencies
p. African Regional Economy Communities (REC) including but not limited to Southern African Development Community (SADC), Economic Community of West African States (ECOWAS); East African Community (EAC), Economic Community of Central African States

5.3 Institutionalization of the Pharmacovigilance Policy Document

Plans shall be put in place to further empower the policy provisions through the appropriate amendment of the Medicines and Related Substance Control Act No. 9 of 2016 within the next five (5) years. The Ministry of Health shall publicise the Pharmacovigilance Policy document and further support the NPC in doing so to all stakeholders. All relevant stakeholders shall be adequately informed and engaged by the end of the first year after launching the policy document. The responsibility for PV shall be shared among multiple stakeholders listed in this policy document. The policy shall be implemented through (an) appropriate plan(s). Strategic areas, objectives, activities, time frame, responsibility and budget where required and the appropriate M&E framework shall be included in the plan(s). National PV guidelines and reporting tools as well as a national sensitization workshop for pharmacy personnel, clinicians and nurses from all facilities shall be implemented. There is also a need to create a standard health care worker training approach and tools to ensure the uniform communication of key messages.

5.4 Pharmacovigilance Structures

The strengthening of an effective and efficient PV structure is an important initial step. It is important to carry out a needs assessment and gap analysis of the existing PV structures. This should be achieved within two (2) years of the policy coming into effect. The NPC structure shall be reviewed depending on the assessment outcome.

5.5 Advocacy and Communication Strategy

The NPC should provide the expertise and carry out advocacy visits and awareness campaigns amongst the decision makers and all the stakeholders as stated

above. The focus on health professionals and consumers should be geared to the identification and forwarding of reports to the NPC and to sustain this, an effective feedback mechanism should be put in place. This would be achieved by workshops, seminars, lectures, etc. and the development of relevant materials for information, education and communication. The media (print and electronic) should be engaged to reach the entire population of consumers with correct and appropriate information on PV. The target of 80% sensitization of the stakeholders should be reached within three (3) years.

5.6 Human Resources Development

5.6.1 Human Resource at NPC

The NPC shall have as Head qualified personnel in PV to run PV activities. The background qualifications and expertise of the personnel shall be in any of the following areas: Medicine, Pharmacy, Clinical Pharmacology, Clinical Toxicology or other related discipline. The complement of the staff in the Unit at any given time shall be informed by the prevailing needs of the Unit to allow the implementation of a strong PV system in the country.

5.6.2 Capacity Building – Personnel and Other Resources

The NPC shall provide a programme for training of personnel in health care facilities and institutions. Such personnel should be knowledgeable in the concept of PV and be able to provide services in the Pharmacovigilance Centre of their respective institution. Short-term in-service programmes should be mounted to achieve a target of 80% coverage of health care facilities in three (3) years and 100% coverage in five (5) years.

5.6.3 Educational and Professional Training

The NPC shall advocate for the development of curriculum and training in PV for undergraduates, postgraduates and health professionals. The implementation shall be achieved by advocacy to the Ministry of Health, Ministry of Education, Eswatini Higher Education Council, Office of Deputy Director Pharmaceutical Services

(ODPPS), universities and academic staff of institutions as well as Professional Councils. Curriculum development and review by the above organizations to accommodate PV in training programs shall be completed within three (3) years of policy implementation.

5.7 Manufacturers/Importers/Market Authorization Holders

Local and multinational importers, distributors and retailers shall comply with existing legislation and guidelines. The NPC shall engage the MAHs to ensure submission of reports as well as Periodic Safety Update Reports (PSURs). Each MAH shall establish an in-house PV Centre to handle PV issues.

5.8 Herbal and Other Traditional Remedies

PV is essential for developing reliable information on the safety of herbal medicines. The Centre will work to change a perception that 'natural' or 'herbal' products are deemed safe simply because they are not synthetic. This thinking leads to virtually no safety monitoring of such product, which may prove detrimental to the health of the general public.

Collaboration between traditional healers and herbalists is therefore needed to bring together the full case. Independent scientific assistance on toxicological investigation and botanical verification shall be done in coordination with universities and other medical expertise. Systematic PV is essential to build up reliable information on the safety of herbal medicines for the development of appropriate guidelines for safe and effective use. In effect, a mechanism for capturing adverse events of medicines in this domain should be properly established.

5.9 Public Health Programmes and Donor Agencies

The Public Health Programmes (PHPs) play an important role in the healthcare system with coverage of many common diseases resulting in the use of a large volume of medicines. The commitment of these programmes to PV is of utmost importance considering the number of persons-administered medicines with a potential for causing ADRs. The NPC shall collaborate with the MOH and PHPs to

institute and streamline PV activities ensuring the regular reporting of medicine-related problems to its database.

PHPs and donor agencies should appreciate the potential impact of medicines donated, and consequently, the need to monitor their safety profile and provide an annual report or more frequent updates in the event of serious ADRs.

5.10 Quality of Medicines

A product registration system and an appropriate quality control testing mechanism should be established within the next five (5) years. Activities to establish a National Medicinal Product Quality Control laboratory should be initiated. This laboratory should also initiate the process of attaining WHO certification. The hazards inherent in illegal cross-border transactions of medicines as well as other practices should be addressed at workshops and other suitable forums, where relevant stakeholders can be engaged and relevant regulatory bodies strengthened to carry out their statutory mandates. The Centre, in coordination with MRU or the MRA once established, shall reduce the prevalence of substandard and falsified medicines within five years. To achieve this, extant laws and sanctions must be duly enforced.

5.11 Research

The NPC, in strong coordination with the Health Research Unit, academia and other key stakeholders, shall collaborate and network to address PV research. In a period not exceeding three (3) years, research focus should address formative issues so as to obtain baseline data in various areas of PV and operational research geared towards enhancing the efficiency of the system. The NPC should also collaborate with other bodies with similar interest such as WHO, USAID as well as other non-governmental organizations.

5.12 Funding

There is a need for independence and integrity of the PV system. The objectivity of the processes leading inputs for decision-making necessitates discretion in the sourcing of funds. The NPC should be funded directly by the Government with an

annual budget. Direct funding from suppliers of medicines will be prohibited for the NPC and all other Centres engaged in PV activities. However, funds may be received from non-governmental not-for-profit outfits.

5.13 Monitoring and Evaluation

The implementation of the Pharmacovigilance Policy requires the erection of structures and the establishment of processes geared towards achieving definite outcomes and impacts. To ensure this, defined monitoring and evaluation mechanisms to measure performance and impact must be put in place. This can be achieved through systematic use of the recently introduced set of PV indicators.

All activities in the National Pharmacovigilance System shall be regularly monitored and evaluated using globally accepted monitoring and evaluation tools. The "Pharmacovigilance Indicators" produced by the World Health Organisation[7] shall be used to assess, monitor and evaluate the PV system. Additionally, the monitoring and evaluation of the PV system shall be included under the Eswatini Pharmaceutical strategic plan.

5.14 Revision of the Policy

This policy shall have a lifespan of ten (10) years after which it shall be revised. Revision of the policy shall be initiated by the National Pharmacovigilance Centre and shall be informed by new developments in the field of PV, changes in policy and legal circumstances in the country and any weaknesses that may have been observed by NPC, staff members and the PV stakeholders in the country.

7 WHO Pharmacovigilance Indicators: A Practical Manual For The Assessment Of Pharmacovigilance Systems: WHO 2015

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