KNOWLEDGE, ATTITUDES, AND PERCEPTIONS OF PHARMACOVIGILANCE AMONG PHARMACISTS IN PHARMACEUTICAL COMPANIES IN SOUTH AFRICA

A Research Report submitted to the Department of Pharmacy and Pharmacology, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Science in Medicine Pharmaceutical Affairs.

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Declaration

I Nkhumeleni Motsage declare that this Research Report is my own, unaided work. It is being submitted for the degree of Master of Science in Medicine Pharmaceutical Affairs at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

…….....
Signature

This …15….day of July 2025… …....

Dedication

To my beloved sister, Khuliso Mathabi who was my greatest believer.

1986 – 2002

May your soul continue to rest in eternal peace.

Acknowledgements

Firstly, I wish to thank the Almighty God for giving me the strength and encouragement to complete this research study.

I wish to thank the following people for the unwavering support, guidance and support towards my studies:

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Abstract

Background: The South African Health Regulatory Authority (SAHPRA) is responsible for monitoring the safety of all medicinal products approved in South Africa (SA). Although it is not legislated for Healthcare Professionals (HCPs) to report adverse drug reactions (ADRs) in SA; however, underreporting of ADRs amongst HCPs remains a concern in SA and understanding the reasons why this is so will provide an understanding on how to resolve this concern. Therefore, the aim of the research was to identify the knowledge, attitudes, and perceptions of pharmacovigilance (PV) among pharmacists in pharmaceutical companies in SA.

Methodology: This qualitative, questionnaire-based study was conducted online using the RedCap tool. The sample size was 162 respondents. Approval from Ethics was received from the University of the Witwatersrand Human Research Ethics Committee (Non-Medical). Data analysis was conducted using Satisfy t-test online calculator.

Results: A total of 85 responses were received, which was a 52.5% response rate. 59 (69.4%) respondents were females and 30 (35.4%) were between 25 and 34 years. 33 (38.8%) respondents have held a position in regulatory affairs and 24 (28.2%) have worked in pharmaceutical organisation for a period between 1 and 5 years. 59 (69.4%) respondents hold a Bachelor of Pharmacy (B.Pharm) completed at local universities (62, 72.9%). 53 (62.4%) respondents received in-house training on management of ADRs and 13 (15.3%) respondents had no additional PV training. The overall knowledge mean score achieved was (85, 72.8%) despite a low correct response on the timelines for reporting suspected ADRs (30, 94.1%) and the Periodic safety update reports (PSUR) / Periodic Benefit Risk Evaluation Report (PBRER) knowledge (37, 43.5%). 84 (98,8%) respondents agreed that reporting of ADRs is an important activity to ensure safety of medicines and 46 (54.2%) believed that educational background has provided them with enough information about ADR reporting. 51 (60.0%) respondents agree that there is adequate PV awareness, however; education through PV conferences was suggested to improve management of ADRs in SA (51, 60.0%). Only 33 (38.8%) respondents have completed an ADR form, and 20 (23.5%) respondents have submitted an ADR report to SAHPRA.

Conclusions: The study highlights the need for more training and awareness on ADRs and PV. While the knowledge of the respondents was fair, this did not translate to ADR reporting amongst this sector. Pharmacists' attitude and perceptions towards the significance of pharmacovigilance in drug development and safety was encouraging.

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List of Abbreviations

ADHD	Attention-deficit hyperactivity disorder
ADR	Adverse drug reaction
AEFI	Adverse event following immunization
ARV	Antiretrovirals
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures
CNS	Central nervous system
EMA	European Medicines Agency
EPI	Expanded Programme on Immunization
EU	European Union
EURD	European Union reference dates
FDA	Food and Drug Administration
FDCA	Food, Drug and Cosmetic Act
HCP	Healthcare professional
ICH 2E	International Conference on Harmonisation
IPASA	Innovation Pharmaceutical Association South Africa
KAP	Knowledge, attitudes, and practices
LMIC	low-to-middle income countries
MAH	Marketing Authorisation Holder
MCC	Medicines Control Council
MCQ	multiple choice questions
MHRA	Medicines and Healthcare products Regulatory Agency
MSc	Master of Science
NADEMC	Adverse Drug Event Monitoring Centre
NDoH	National Department of Health
OUD	opioid use disorder
PBER	Periodic Benefit Risk Evaluation Report
PIDM	Programme for International Drug Monitoring
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic safety update reports
PV	Pharmacovigilance
QA	Quality Assurance

RA	Regulatory Affairs
SA	South Africa
SAAPI	South African Association of Pharmacists in Industry
SAHPRA	South African Health Products Regulatory Authority
SAPPRA	Southern African Pharmaceutical Regulatory Association
TSR	Targeted Spontaneous Reporting
TSR	Targeted Spontaneous Reporting
UMC	Uppsala Monitoring Centre
USA	United States of America
WHO	World Health Organisation

Chapter 1 Introduction

1.1 Background

The use of diethylene glycol as a solvent for sulfanilamide was linked to 107 fatalities in 1937 (The Lancet, 1998). After learning that chloroform was a more potent and safe anaesthetic, Sire James Simpson, a professor of midwifery at Edinburgh, implemented it in clinical settings. However, Hannah Greener, a small child from the the North of England, passed away following the excision of an infected toenail after being given a chloroform anaesthetic. Clinicians and members of the public have voiced concerns regarding the safe use of chloroform as an anaesthetic (Fornasier *et al.,* 2018).

Subsequent to this, in 1961, Dr. McBride, an Australian doctor, wrote a letter to the editor of the Lancet Journal, in which he suggested a connection between congenital malformation of babies and thalidomide. In fact, he observed that the incidence of congenital malformations of babies (1.5%) had increased up to 20% in women who had taken thalidomide during pregnancy (Fornasier *et al*., 2018). These tragedies sparked discussions around medicine safety which then resulted in the establishment of the World Health Organisation (WHO) Programme for International Drug Monitoring (WHO, 2002).

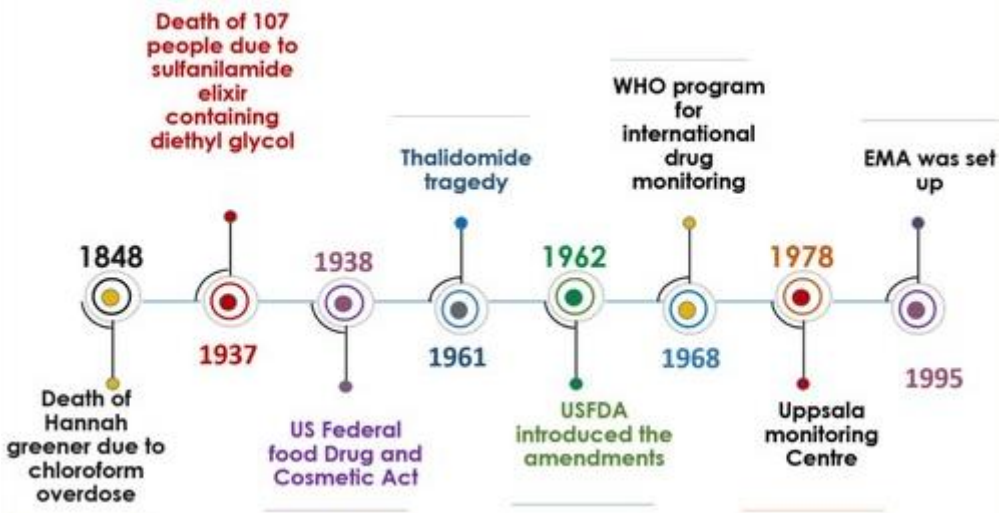


Figure 1.1 historical overview of pharmacovigilance (Khan *et al*., 2024).

Pharmacovigilance system has experienced numerous changes since its establishment. The 16.36 resolution at the 16th World Assembly advocated for a systematic gathering of data on major adverse drug reactions (ADRs) during the development of medications and especially when they are released for general use.

The WHO's Programme for International Drug Monitoring (PIDM) was established as a result of this resolution (Khan et al., 2024).
Historically, physicians were the only professionals assessing whether a disease or medicine caused certain symptoms. It was argued that only allowing doctors to submit ADR reports would guarantee high-quality data and reduce the reporting of random and irrelevant events. Research has indicated that various types of medical practitioners will observe various drug-related issues (WHO, 2002).

In South Africa, ADR reporting practices and requirements are outlined in the guideline for adverse drug reactions (ADRs) reporting for healthcare professionals. The ADR guideline includes the requirement for a healthcare professional to inform South African Health Products Regulatory Authority (SAHPRA) of any suspected ADRs or new or existing safety, quality or effectiveness concerns occurring because of the use of any medicine or scheduled substance (www.sahpra.org.za, 2020).

ADR reporting guideline is generally followed, however; according to literature review, ADR underreporting by healthcare professionals is a worldwide problem (Segomotso and Ntuli-Ngcobo, 2011). According to a 2022 study on adverse drug reactions, underreporting of suspected ADRs is one of the largest problems facing pharmacovigilance worldwide and in South Africa (Viljoen and Muntingh, 2022). A research study conducted in United Kingdom (UK) confirmed that lack of time and ADRs considered not serious enough by pharmacists to report were barriers to ADR reporting. Further training and education about types of ADRs to be reported can help to improve the reporting of ADRs (Cheema *et al*., 2017). A research study on profile of adverse drug reaction reports in SA concluded that ADR reporting by pharmacists was lowest among healthcare professionals (Matlala *et al.*, 2017). The common factor identified was inadequate knowledge level towards pharmacovigilance. A research study by Rikhotso *et al.* conducted in SA suggested that (PV) training on how to detect potential ADRs, will indeed impact ADR reporting (Rikhotso, 2021). A study by Joubert and Naidoo confirmed that the majority of pharmacists are willing to go for further education to improve ADR reporting in SA (Joubert and Naidoo, 2015). Knowledge level of the study respondents to ADR reporting was inadequate. Answers towards ADR reporting form and related processes were not satisfactory (Bogolubova *et al*., 2018).

1.2 Research question

What are the knowledge levels, attitudes, and perceptions of pharmacovigilance among pharmacists working in pharmaceutical companies in South Africa?

1.3 Problem Statement

Underreporting of ADRs by pharmacists to Adverse Drug Event Monitoring Centre (NADEMC) and SAHPRA is a challenge in South Africa and worldwide problem (Segomotso and Ntuli-Ngcobo, 2011). Pharmacists' role in ADR reporting is vital in ensuring drug safety by detecting and reporting ADRs. Sir James Simpson had discovered that chloroform was a safer and powerful anaesthetic, and he had introduced it in clinical practice (Fornasier *et al.,* 2018). The research study was on the knowledge, attitudes, perceptions and current practices of pharmacovigilance among pharmacists in pharmaceutical companies in South Africa.

1.4 Rationale and motivation

South Africa's SAHPRA regulations for post-marketing reporting of adverse drug reactions (ADRs) focus on both reporting and monitoring ADRs. ADR reporting remains an effective means to identify significant, uncommon, or previously identified ADRs. Product safety information can change as a result of ADR monitoring trends, supporting regulatory decisions to remove a product from the South African market. All South Africans benefit from the information that ADR reporting in SA contributes to global data on medication risks and efficacy as well as the dissemination of health product safety knowledge (www.sahpra.org.za, 2020).

Pharmacovigilance together with any drug safety concerns are relevant (WHO, 2002). Pharmaceutical products undergo safety reviews in order to provide a thorough and critical analysis of the product's risk-benefit balance. These reviews take into account newly discovered safety information in the context of cumulative information on risk benefits and, when necessary, implement risk-reduction measures. Clinical trials aimed at determining a pharmaceutical product's safety and efficacy are included in safety evaluations of pharmaceutical products (www.sahpra.org.za, 2020).

According to literature review, there is a limited number of research studies previously conducted to establish knowledge, attitudes and perceptions towards PV among

pharmacists in pharmaceutical companies. Results of this research will demonstrate the knowledge level of pharmacovigilance among pharmacists in pharmaceutical companies in South Africa. The research results will also demonstrate pharmacists' attitude and perceptions towards pharmacovigilance and current practices of ADR reporting among pharmacists in various roles within the pharmaceutical organisation in South Africa.

1.5 Aims and Objectives

The aim of the research was to identify and describe the knowledge, attitudes, and perceptions of pharmacovigilance among pharmacists in pharmaceutical companies in South Africa.

1.5.1 Objectives

1. Evaluating the level of knowledge about pharmacovigilance among pharmacists in pharmaceutical companies in South Africa.
2. Assessing the attitudes of pharmaceutical industry pharmacists towards pharmacovigilance practices.
3. Exploring the perceptions of pharmaceutical industry pharmacists on pharmacovigilance practices.
4. Comparing the knowledge, attitude and practice (KAP) of pharmacists in pharmaceutical companies and determining if there were associations between the respondents' knowledge, attitudes, and perceptions of pharmacovigilance with their age, years of experience and job roles.

1.6 Outline of this Research Report

Figure below to illustrate the sections contained in this research report:

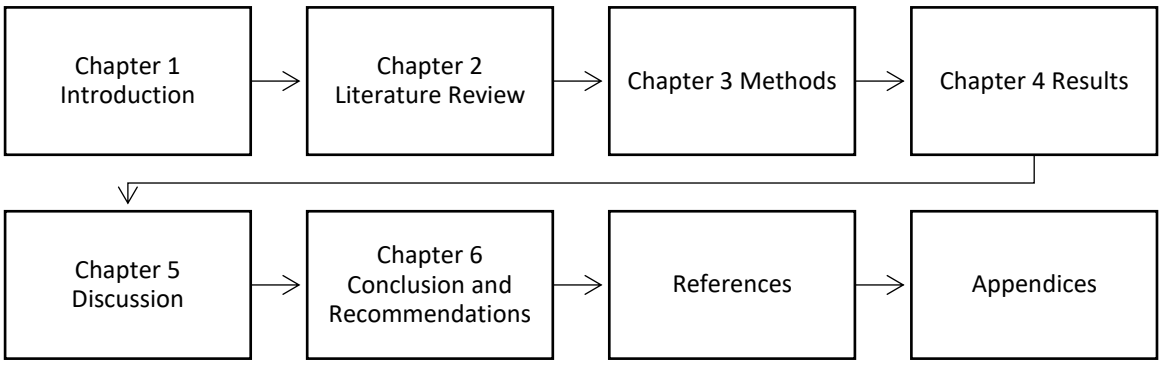


Figure 1.2. Outline of the research report

Chapter 2 Literature Review

2.1 Introduction

This chapter outlines an overview of the literature review conducted on previously completed published literatures. The review included summarising published works related to the research topic theories and concepts also highlighting gaps and critical reflections on pharmacovigilance and adverse drug reporting processes. The literature review aims to address the research question.

2.2 Drug development

2.2.1 Discovery and development

According to South Africa's Medicines and Related Substances Act 101 of 1965, a medicine is any substance or combination of substances that is used, manufactured, or sold for use in:

> (a) the diagnosis, treatment, mitigation, modification or prevention of disease, abnormal physical or mental state, or the symptoms thereof in man; or
> (b) restoring, correcting, or modifying any somatic or psychic or organic function in man; and includes any veterinary medicine (Act 101, 1965)

Pre-clinical research testing (*in-vitro and in-vivo*), clinical research, regulatory agency evaluation, post-market safety monitoring, and discovery and development constitute the drug development process. About 70% of phase I trials will produce positive results and proceed to phase II trials, which enrol more participants while maintaining side effects and efficacy. Only one-third of the drugs proceed to the next stage of clinical trials, which entails recruiting a sizable participant base over a lengthy period of time in order to track adverse drug reactions and the drug's effectiveness. Approximately 30% of phase III trials are approved by the FDA, while phase IV studies are followed up on after market approval (Salib, 2023).

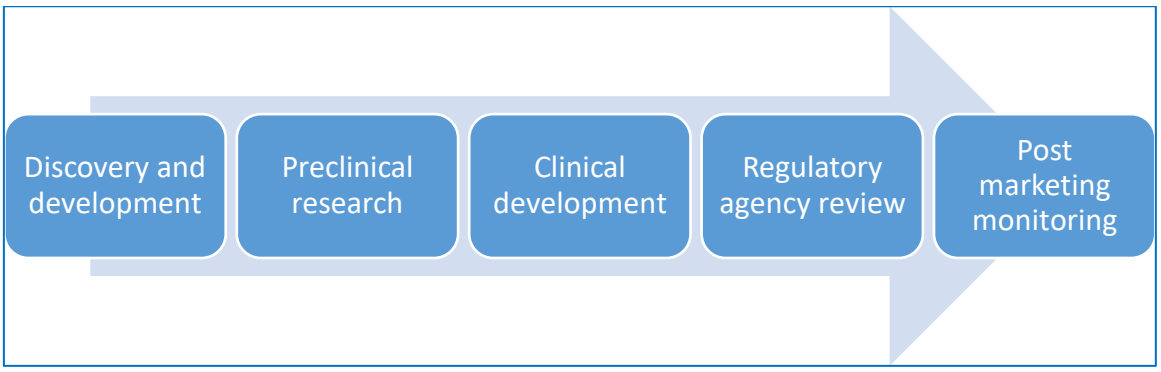


Figure 2.1: Steps of drug discovery and development (Salib, 2023).

2.2.2 Drug safety

The South African Health products Regulatory Authority (SAHPRA) plays a pivotal role in overseeing the regulation of all medicines within South Africa, ensuring that all medicines meet safety, efficacy and quality standards. The SAHPRA is also responsible for drug approval and registration, monitoring safety and compliance of medicines and issuance of safety alerts and guidelines to healthcare providers in both private and public sectors within South African borders (www.sahpra.org.za, 2020).

According to a Louis et al. study on evaluating a structured, quantitative health outcomes approach to medication risk-benefit analysis, regulatory evaluation of a new treatment at the pre-approval stage should balance the drug's anticipated safety risks against its anticipated positive health effects (Louis *et al.*, 2007).

2.3 Pharmacovigilance

Pharmacovigilance, according to the World Health Organization, “is the science and practice of identifying, evaluating, understanding, and preventing side effects or any other issues pertaining to medicines”. Pharmacovigilance objectives according to WHO are:

- To enhance public health and safety regarding medication use.
- To enhance patient care and safety regarding the use of medications and all medical interventions.
- To identify issues with taking medicines and promptly report the results.
- To help evaluate the risks, benefits, harm, and effectiveness of medicines in order to minimize harm and maximize benefit

- To promote the safe, practical, and efficient use of medicines, including cost-effectiveness.
- To advance knowledge, instruction, and clinical practice in pharmacovigilance and public outreach (WHO, 2002).

2.3.1 History of Pharmacovigilance

Following severe side effects from administering Thalidomide to pregnant women, pharmacovigilance was officially established in Great Britain in 1961. There were multiple cases of fetal abnormalities. Medicinal drug surveillance began with this significant incident. But the history of pharmacovigilance was also influenced by several other incidents. According to literature, the first pharmacovigilance cases involving chloroform were documented in 1848 (Khan *et al.*, 2024)

2.3.1.1 1848 – Chloroform

Pharmacovigilance began in 1848 after a number of mysterious fatalities in Great Britain during procedures where patients received chloroform as an anaesthetic. The Lancet Journal formed a panel and encouraged British doctors to report such events after a 15-year-old girl died following receiving chloroform as an anaesthetic for the first time in 1847. As a consequence, there was a debate over the safety of anaesthetic treatments, and in 1976, the substance was no longer used as an anaesthetic due to a number of incidents (Fornasier *et al.,* 2018).

2.3.1.2 1937 – Sulfanilamide

A new liquid formulation of Sulfanilamide that contained the solvent Diethylglycol as a diluent which caused fatal reactions killed 107 individuals in the United States in 1937, including 76 babies. The toxicity was unknown to the manufacturing company. This tragedy made evident how important it is to ensure the safety of the drug's excipients as well as its active ingredient (Khan *et al*., 2024).

2.3.1.3 1961 – Thalidomide

The use of Thalidomide in pregnant women, which resulted in congenital deformities in fetus, was the decision that led to the development of PV in 1961. For approximately two years, Thalidomide was tested on a large number of individuals with no negative effects found. As a result, it was seen as a safe drug that was mostly used to sedate

pregnant women. More than 10,000 infants were born with severe limb abnormalities. The catastrophe led to the development of spontaneous ADR reporting in Europe (Safety drugs pharmacovigilance solutions, 2024 and Fornasier *et al.,* 2018).

2.3.2 Birth of Regulatory bodies

The United States Food and Drug Administration (FDA) was given the power to regulate the safety of food, medications, medical devices, and cosmetics in 1938 when the Food, Drug, and Cosmetic Act (FDCA) was created. The World Health Organization (WHO) was founded in Geneva, Switzerland, in 1948.

When the Food, Drug, and Cosmetic Act (FDCA) was passed in 1938, the FDA was granted the authority to oversee the safety of food, pharmaceuticals, medical devices, and cosmetics in the United States. Following the Thalidomine catastrophe, the United States introduced the Harris-Kefauver amendments in 1962, requiring preclinical investigations to be conducted. The clinical trial phase on humans could only begin when the outcomes of these studies were evaluated. Additionally, the information gathered during the clinical trials three phases was necessary for the marketing authorisation. Drugs were subjected to post-marketing surveillance after they were released to the market. In 1978, the WHO and the Swedish government established the Uppsala Monitoring Center (UMC) (Safety drugs pharmacovigilance solutions, 2024 and Fornasier *et al.,* 2018).

The World Health Organization's collaboration center for international drug monitoring is known by its field name, the UMC. The UMC's main responsibility is to oversee the global database of ADR reports that are submitted by National Centers. Nearly three million case reports were stored in this database in 2002. To encourage quick signal detection, the UMC has standardised reporting by all National Centers and enabled international communication between countries (WHO, 2002).

2.3.3 Scope of pharmacovigilance

Pharmacovigilance's primary objective is to encourage the safe and efficient use of medicinal products, by promptly informing patients, healthcare professionals, and the general public about the safety of medicines. Therefore, pharmacovigilance is an activity that contributes to protect patients and maintain public health (Nour and

Gilles Plourde, 2019). Scope of pharmacovigilance is problems resulting from any of the following or a combination of any of the following:

- pharmacovigilance includes elements such irrational drug use, overdoses, illicit trade of medicines and drugs of abuse online, growing self-medication, substandard medications, medication errors, and ineffectiveness (WHO, 2002).

Figure 2.2. below illustrates the different sources where information about safety can be obtained from (Tim, 2016).

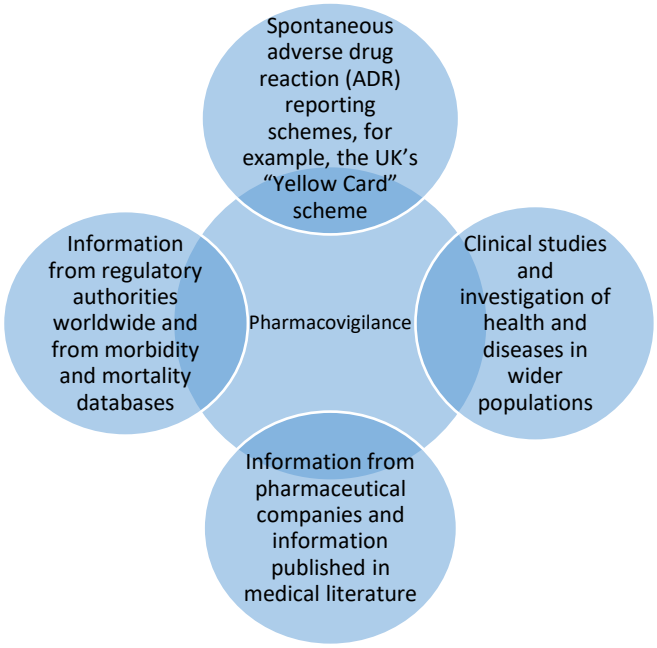


Figure 2 .2: Sources of information (Sandle and Tim, 2016).

2.3.4 Pharmacovigilance methods of reporting

Analytical or descriptive studies can be carried out at the post-marketing stage. Intensive monitoring studies and spontaneous reporting systems (SRS) are examples of descriptive research. These are significant in formulating theories that are later analysed. Cohort and case-control studies are examples of analytical studies (Rikhotso, 2021).

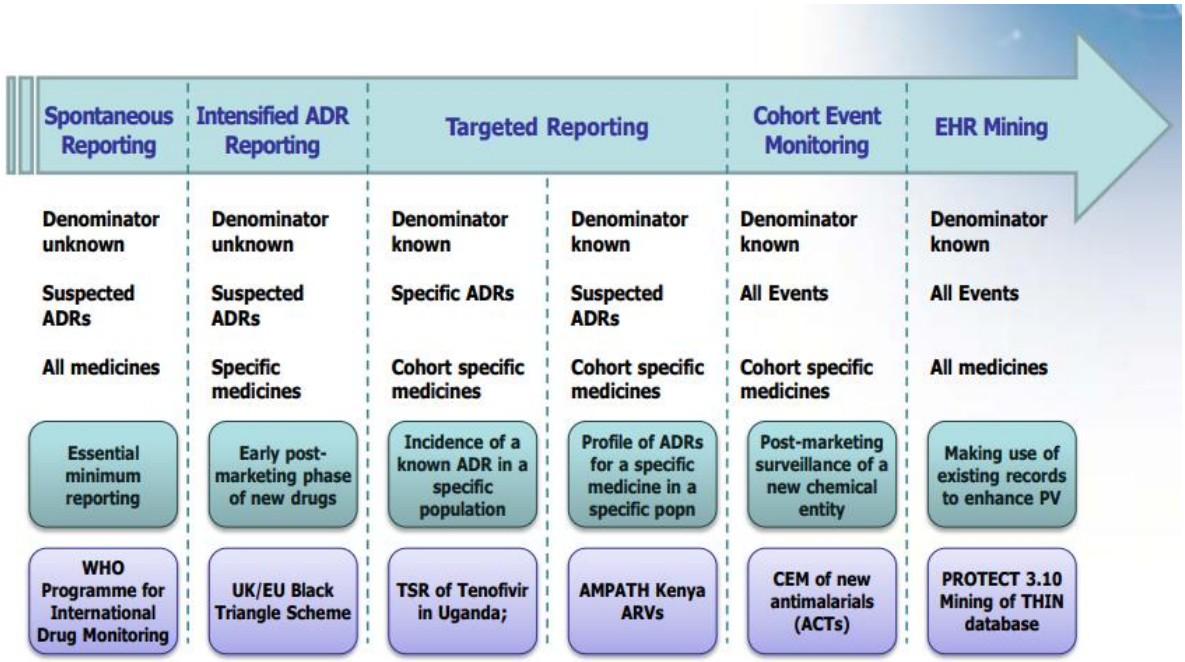


Figure 2.3: PV methods spectrum figure from the Uppsala monitoring centre (Hill, 2025).

2.3.4.1 Spontaneous reporting system

A process in which healthcare professionals and pharmaceutical manufacturers voluntarily submit case reports of adverse drug events to the national regulator is referred to as spontaneous reporting (WHO, 2002).

By its true nature, spontaneous reporting is a passive method of pharmacovigilance (PV), depending solely on the willingness of individuals to notify a local or national pharmacovigilance center about potential adverse drug reactions (ADRs) (Schurer, 2019). Reporters' involvement determines whether any spontaneous reporting system succeeds or fails. Throughout the history of pharmacovigilance, healthcare professionals have been the primary source of case reports of suspected ADRs, despite the recent introduction of limited patient reporting schemes (WHO, 2002).

Although voluntary at the point of treatment of patients, the backbone of the national PV system is the spontaneous reporting of suspected adverse drug reactions (ADRs) by pharmaceutical companies and healthcare professionals (HCPs). HCPs' professional accountability, initiative, drive, and participation constitute the basis of the spontaneous ADR reporting system (Desai, 2022).

Spontaneous reporting significantly impacts drug approval processes and post-marketing actions as it informs regulatory agencies about the actual use of drugs in diverse populations. Reporting of serious ADRs can lead to intensified scrutiny, label

modifications, or even withdrawal of a drug from the market. By analysing spontaneous reports, agencies can make informed decisions that protect public health and ensure that medications remain safe for use in the general population (Schurer, 2019).
Even though the cornerstone of passive monitoring is spontaneous reporting, the data collected is naturally limited and is likely not adequate for clinical and regulatory decisions. Drug safety risks have been effectively identified and quantified through active or intense surveillance programs designed to address major safety concerns (WHO, 2002).

2.3.4.2 Intensified ADR reporting

The goal of intensified ADR reporting is to enhance certain pharmaceutical medications in the early post-marketing stages. Biological medicines, medicines with a new active ingredient, medications with conditional approval or approval under special conditions, and medications that need more research are all considered to be "under additional monitoring" (Hill, 2025).

In contrast to spontaneous reporting, which tracks specific medications over a predetermined amount of time, extensive monitoring is based on a non-interventional observational cohort. Intensive monitoring offers real-world clinical data that does not involve inclusion or exclusion criteria during the collection period due to its non-interventional nature. Selection bias is eliminated since it is not impacted by the types of exclusion and selection criteria that define clinical studies (Härmark and Grootheest, 2008).

2.3.4.3 Targeted Spontaneous Reporting (TSR)

The advantage of TSR is that it can effectively use already established infrastructure, its focus is on specific medicines and all the required necessary information is captured. Targeted spontaneous reporting focusses on specific medicines or reports, this is also a disadvantage as some reports can be missed (Hill, 2025).

2.3.4.4 Cohort event monitoring (CEM)

Defined by the WHO as the use of prospective, observational cohort studies of patients who have received the relevant medicine. Not just suspected adverse reactions, but all adverse events are documented in the study. In light of this, the method is especially efficient at detecting unfavourable reactions that were previously unknown and

unexpected (WHO, 2006). Cohort event monitoring's goal is to understand more about a new chemical entity's safety profile in the early post-marketing stage *(*Hill, 2025).

2.3.4.5 Electronic Health Records (EHR) mining

In EHR mining, existing health records are used to supplements pharmacovigilance activities. The UK established the General Practice Research Database (GPRD), which captures useful data including patient demographics, medical histories, hospital referrals, drug dispensing, vaccination records and lab results (Rikhotso, 2021).

A study by Davis *et al.* concluded that despite broad interest in utilising EHRs for safety signal identification, current efforts fail to leverage the full breadth and depth of available data or to rigorously control for confounding. The development of best practices and application of common data models would promote the expansion of EHR-based pharmacovigilance (Davis *et al.,* 2023).

2.3.5 Adverse Drug Detection, Processing and Reporting

2.3.5.1 Adverse Drug detection

An undesirable drug experience is defined as failure to produce expected benefits (Gliklich *et al.,* 2014). Tables 2.1 – 2.4 outlines examples adverse events (AE) types.

Table 2.1: Failure to produce expected benefits – lack of efficacy.

Lack of efficacy	**Examples of AE type**
According to prior scientific research, the World Health Organization defines lack of efficacy as a drug's unexpected failure to produce the expected outcome (WHO, 2002).	Important information about such circumstances can be obtained from findings of unexpected ineffectiveness in patients. As a result, ineffectiveness is a potentially significant reportable event in pharmacovigilance, particularly when it occurs unexpectedly or without explanation (Meyboom et al., 2000). In some situations, disclosing treatment ineffectiveness could help find deficiencies in medicines. However, implementing suitable production processes and increasing quality control efforts would be the robust method to prevent this from occurring (Figueras, 2002).

Table 2.2: Off-label use.

"Off-label" Use	Examples of AE type
Unapproved use of approved drugs often called "off-label" (FDA, 2018) The term "off-label" can mean that the drug is: • Utilised to treat a medical condition or illness for which it is not authorised. • Administered in a different manner, such as when a medication that is authorised for use as a capsule is administered as an oral solution instead. • Administered at a different dosage, for example, when a medication is prescribed by a doctor to a patient at a dose of one tablet daily, but the patient is instructed to take two tablets daily (FDA, 2018).	Concerns have been raised over the inadequacy of research on off-label and unlicensed procedures in developing nations including South Africa. This is despite knowing that these practices are well-characterised in numerous developed countries and areas (Ngcobo and Mathibe, 2024). Examples of medicines commonly prescribed as an off-label medication: • Tretinoin or Retin-A is licenced to treat acne but is often prescribed off-label for anti-aging and hyperpigmentation treatment (City Skin Clinic, 2025). • In 1994, the FDA authorised the clinical use of gabapentin as an additional medication for adults with epilepsy who experienced partial seizures. In epileptic individuals, gabapentin decreases neuronal excitability. However, it is sometimes suggested to treat migraine, bipolar disorder, and neuropathic pain (Ngcobo and Mathibe, 2024). • Although Prazosin (Minipress) for Nightmares has been approved for the treatment of hypertension, it is also used to treat PTSD-related nightmares. The treatment of Raynaud's illness and poisoning from scorpion venom are additional non-FDA-approved uses for prazosin (Pharmacy Times, 2016). • When marketed under the Wellbutrin brand, bupropion is prescribed to treat depression. It is also marketed under the name Zyban as a medication to help people quit smoking. Provincial drug insurance in Ontario, Canada, do not cover smoking cessation medications. Therefore, a doctor can prescribe Wellbutrin to help people quit smoking (Wikipedia, 2025). • Revia, or Naltrexone, is used to treat behavioural addiction. Despite initially prescribing Naltrexone to treat opioid addiction, doctors are now using the medication in off-label manner to help patients with everything from pain and immune system malfunction to inflammation, cancer, and mental health disorders (Weill Cornell Medicine, 2020).

Table 2.3: Medication errors.

Medication errors	Examples of AE type
A "medication error" is defined by the US National Coordinating Council for Medication Error Reporting and Prevention as any avoidable incident that could result in inappropriate pharmaceutical usage or harm to people when a medicine is in the possession of patients, healthcare professionals, or consumers. Professional practice, healthcare items, procedures, and systems, such as prescription writing, ordering medicines interactions, product labelling and packaging, medicine preparing, distribution, administration, education, monitoring, and use, can all be connected to these events (Mistry et al., 2023). When the processes of prescribing, transcribing, dispensing, administering, and monitoring medications are impacted by human factors like fatigue, unfavourable working conditions, or a shortage of staff, medication errors can result in severe injury, disability, and even death (WHO, 2025). Both hospitalised and non-hospitalised patients have a well-documented history of medication mistakes and adverse drug reactions (ADRs), which significantly increase mortality and morbidity (WHO, 2002). According to reports, the third most common cause of death in the US is medical errors. Using expired medications, providing a medication that looks similar, or neglecting medication-use safeguards are examples of common pharmaceutical errors (Rodziewicz et al., 2024). Medication errors are caused by a number of causes including those pertaining to the	• Following a prescription error, the woman's skin melts off. An antidepressant patient who was given the incorrect dosage developed Stevens-Johnson syndrome, which caused her skin to completely melt off. The 26-year-old woman's skin was burned and scarred, her sweat glands melted, her fingernails stopped growing, and her vision was gradually deteriorating (Bertram and Murphy, 2021). • Diabetic Woman Given Insulin Against Doctor's Orders. ER doctor and nurses ordered and administered excessive doses of insulin and failed to properly monitor blood sugar levels post-administration of insulin resulting in death of 46-year-old woman (Lubin and Meyer, 2015).

patient, the healthcare professional, and the system (Mistry et al., 2023). • Patient related factors According to the FDA, people 60 years of age or older are the most vulnerable to drug errors, with over half of fatal pharmaceutical errors occurring in this age group (Sears et al., 2012). According to WHO research, 70% of nursing home patients had a prescription error, and 9% of all prescribing events in nursing homes involved errors. Medication errors were caused by a variety of factors, such as medical conditions that made administering prescriptions challenging and misinterpretation or misunderstanding of treatments (WHO, 2016). • Healthcare provider related factors Lack of therapeutic training, insufficient pharmacological knowledge and expertise, insufficient patient education, insufficient risk awareness, overworked or worn-out medical staff, physical and mental health problems, and poor patient-provider communication are all factors associated with medication errors (WHO, 2016). In primary and outpatient healthcare, up to 40% of people worldwide experience harm. Preventable harm accounts for as much as 80% of this figure. The most harmful mistakes are associated with the diagnosis, prescription, and administration of medications. Adverse events account for 15% of total hospital activity and expenses in OECD countries (Mistry et al., 2023). • System related factors Complicated processes for generating original prescriptions, unclear procedures for generating accurate repeat prescriptions, inaccurate patient records, and poor design that promotes human mistake are some of the	

factors that may contribute to system-related drug errors (WHO, 2016).	

Table 2.4: Misuse, including drug overdose, whether accidental or intentional.

Misuse	Examples of AE type
Prescription drug abuse includes taking prescription medicines from someone else, even if they are prescribed for a valid medical condition like pain, using a medication to feel happy, or using a medication in a way or quantity that is not advised. Central nervous system depressants, opioids, and stimulants are the three drug classes most commonly abused (NIDA, 2023).	• Typically, opioids are prescribed for reducing pain. Pain reduction is one of the many effects that opioids have on the brain. Opioids include both illicit and prescribed painkillers. The “high" effect created by taking Opioids Is why many people use it. that opioids can create is the reason why some people use them (Hopkins, 2025). Opioids can cause severe respiratory depression, which is the slowing or stopping of breathing, even with a single large dose. This risk is increased when opioids are taken with alcohol or sedatives. (NIDA, 2023). • Sleep and anxiety disorders are treated with central nervous system (CNS) depressants. Benzodiazepines, non-benzodiazepine medications for sleep, and barbiturates are some of the drugs that are frequently used for these purposes (NIDA, 2023). CNS depressant drugs have the potential to enhance quality of life when used as prescribed by a doctor. An increase in reliance on CNS depressive drugs could lead a way for addiction. A lack of oxygen to your brain, or hypoxia, can result from a CNS overdose. Death, coma, severe brain injury, and seizures (Melinosky, 2023). • Most frequently, stimulants are utilised to treat ADHD, or attention-deficit hyperactivity disorder. In addition to raising blood pressure, heart rate, and breathing, stimulants can boost energy, alertness, and concentration. Stimulants are used to treat fewer illnesses now that their potential for abuse and addiction has been identified. Presently, stimulants are only used to treat a small number of illnesses, such as narcolepsy, attention-deficit hyperactivity disorder (ADHD), and occasionally depression that is resistant to treatment (NIDA, 2023).

	• Anxiety, tension, elevated body temperature, nausea, tremors, seizures, coma, and death can all result from higher stimulant dosages (Talcherkar, 2025).

2.3.5.2 Adverse drug processing and reporting

The public and healthcare professionals can report suspected adverse drug reactions (ADRs) through the reporting methods found in most national pharmacovigilance systems. Online portals, smartphone applications, toll-free hotlines, and paper-based forms are all options for reporting. These systems promote the prompt and accurate reporting of drug-related adverse events (Tadge *et al.*, 2023).

When developing a standard ADR reporting form that will accommodate the wide variety of reports that a national PV center must receive, a one-size-fits-all approach is inadequate; yet some information will always be required. Patient demographics, drug use, events, and reporters are examples of standard information (in case extra information is required). Only age, gender, race, and medical history are collected for patient demographics; no personally identifiable information is collected. Knowing the suspected drug, indication, dosage, action taken, concurrent drugs, and how the suspected adverse drug reaction was handled are all helpful when it comes to drug use. Sometimes taking a medication for incorrect reasons or at the wrong dosage can result in an undesirable effect. Comorbidities may also be revealed by concurrent medication. Information on the event's nature, start and end dates, treatment, and circumstances are useful (to be able to identify any medication errors, counterfeit medicines, etc.) (Rikhotso, 2021).

The responsibility for reporting adverse events falls on several key players in the healthcare system:

- Manufacturers: Drug and device manufacturers are legally required to report adverse events to the FDA. This includes both prescription and over-the-counter products, as well as biologics and medical devices.
- Healthcare Professionals: While not legally required to report, healthcare providers play a crucial role in identifying and reporting adverse events. They are often the

first to observe adverse reactions in patients and can report these events to the manufacturer or directly to the FDA.

- Consumers: Patients and consumers can also report adverse events directly to the FDA through the MedWatch program. While voluntary, consumer reports are valuable in identifying potential safety issues (All about pharmacovigilance, 2025).

2.4 Substandard and falsified (SF) medical products

Products that do not meet specifications are known as SF mediations, and they often arise from substandard manufacturing processes or inadequate quality control (WHO, 2024).

Drug SF has a centuries-long history and is regarded as one of the most ancient crimes in human history. There have been references to a supply of fake antimalarials for many years, including quinine in the 1800s and cinchona in the early 1600s (Pathak et al., 2023). Millions of people are affected by SF medical products, which create serious risks to global health systems. These products are present in each country and have an effect on every aspect of medical supplies, including cancer treatments, vaccines, and antibiotics (WHO, 2024). Given the pain and suffering they inflict on people and the extra burden they put on the healthcare system, SF medications often present a threat to public health. Because of the harmful ingredients they contain, SF medications have the potential to seriously harm health or worsen the conditions that they are intended to treat. In a single case, it was stated that unintentional pregnancy resulted from the theft and sale of placebo tablets lacking active ingredients as a form of birth control (WHO, 2006).

According to a 2017 WHO estimate, approximately 10.5% of drugs worldwide are SF. A study found that in developing countries, the overall incidence of SF was approximately 13.6%. In this instance, the expected economic impact might reach $200 billion (Pathak *et al*., 2023).

Due to insufficient infrastructure and resources in many countries, particularly in low- and middle-income nations, SF healthcare products are hard to address (WHO, 2024).

Different countries have different laws to discourage SF. Respective governments can play a crucial role in providing financial budgets to the health agencies to support active drug surveillance. Further from Pharmacovigilance aspect, procuring data regularly by

encouraging pharmacy and consumer to report information when drug is not proven to be effective will help drug manufacturer save their drugs by reporting accurate information to agencies. To effectively manage danger posed due to counterfeit drugs, collaboration at global level including nations, pharmaceutical companies and regulatory bodies will be the game-changer (Pharmavector, 2024).

2.5 Global pharmacovigilance awareness

The World Health Organization has a mandate to develop, establish, and promote international standards relating to food, biological, pharmaceutical, and other related products, as stated in Article 2 of the World Health Assembly's constitution. Additionally, Article 21 of the World Health Assembly's constitution provides for the adoption of rules relating to the potency, safety, and purity of pharmaceutical, biological, and similar products that are distributed internationally (WHO, 2002).

The WHO and other collaborators aim to advance health education on a global scale in order to improve PV communication and awareness (Rikhotso, 2021).

In 1968, the WHO developed the WHO Programme for International Drug Monitoring (WHO PIDM). The objective of WHO PIDM is to assure identification of safety issues relating to vaccines and drugs. About 99% of the world's population is protected by this program, which has more than 180 total members and affiliated members. Since 1978, the Uppsala Monitoring Center has been in charge of the WHO PIDM's operational aspects in its role as the WHO Collaborating Centre for International Drug Monitoring (WHO PIDM, 2025).

International health cooperation in the Americas is overseen by the Pan American Health Organization (PAHO), a specialized agency of the United Nations (UN). It encourages technical collaboration among member nations to fight communicable and noncommunicable diseases, develop health systems, and respond to emergencies and disasters. PAHO was established in 1902 and currently includes four Associate Members and 35 Member States across the region (PAHO, 2011).

Systems of pharmacovigilance are not perfect. Latin America and the Caribbean's pharmacovigilance programs are still in their infancy and faces the same challenges as developed nations: underreporting, unnecessary reporting of known adverse

reactions, conflicts of interest resulting from prescribers' and dispensers' relationships with pharmaceutical companies and a lack of incentives for healthcare professionals to report (PAHO, 2011).

In order to meet the requirements of society as a whole, pharmacovigilance and its practices must continue improving. Three studies in particular have been essential in recent years for offering perspective of pharmacovigilance's future. Global pharmacovigilance agencies developed strategies for risk communication. According to PAHO, risk communication includes Periodic Safety Update Reports, Publication and Information in Pharmacovigilance and Crisis Management (PAHO, 2011).

2.5.1 Periodic Safety Update Reports (PSUR)

Periodic safety update reports are formal documents that include all of the pharmacovigilance information for a specific medication over each period according to the date of registration. Pharmaceutical laboratories are required to take part in the reporting data compilation, assess the safety information gathered, and submit it to the regulatory agency that authorised the drug in a standard way. The national and global experience with medication safety is presented in these studies (PAHO, 2011).

MAHs face challenges when gathering data that need to be prepared and submitted to authorities as these data comes from various sources and requires analysis before submitting. Types of data sources include clinical trials, post market surveillance and medical literatures. MAHs need to adhere to the timelines for submission of PSURs to the authorities, collaboration with various stakeholders is essential. The other challenge MAHs face is on the various standards and associated templates or formats from various countries that need to be standardised before PSUR submission (DDReg Pharma, 2025).

2.5.2 Publication and Information in Pharmacovigilance

Risk information on medicines should be released and shared promptly. Following evaluation, this information should be distributed to the general public via the proper channels. Healthcare professionals, holders of marketing authorisations, pharmacovigilance systems or other organisations, and the medicines regulatory authorities should all be informed as soon as possible about potential adverse reactions (PAHO, 2011).

2.5.3 Crisis Management

In April 2023, WHO launched a new initiative to help nations better prepare for future pandemics by providing guidance on integrated preparedness for responding to any respiratory infection, including influenza or coronaviruses. The new Preparedness and Resilience for Emerging Threats Initiative, or PRET, incorporates the most up-to-date methods and resources for public education and behaviour that were created during the COVID-19 pandemic and other recent public health events (WHO, 2023). When news breaks regarding vulnerabilities with a product's efficacy or safety that could seriously affect public health and urge quick action, a crisis may arise. Reports in the media voicing concerns about the use of a specific product might potentially trigger a crisis. In the event of a crisis, the regulatory agency should review the information at hand and use it to guide the decisions that need to be taken. These decisions may include applying the proper regulations, acquiring or publishing more information, and communicating the danger or lack thereof. In any event, stakeholders should work closely together, and emergency actions should be ready to be implemented when there is confirmation of concern or harm and potential effects on public health (PAHO, 2011).

The objective of the EMA health threat plan is to offer general internal guidelines for EMA operations both before and during a public health emergency. In order to incorporate any existing systems or processes that might be used during such a crisis, the health threat plan and related documents are based on the experience obtained from what may be considered the most likely cause of an emerging health threat, namely a biological health threat, and in particular a respiratory virus with pandemic potential (EMA, 2022).

2.6 African Pharmacovigilance awareness

Decisions concerning health policy in the African region are made by the WHO Regional Committee for Africa. It is made up of the health ministers or their representatives from each of the region's 47 member states. According to Article 50 of the WHO Constitution, the Regional Committee's primary responsibilities include overseeing the regional office and developing regional policies. Every five years, the Committee officially selects the Regional Director for Africa and submits the selection to the WHO Executive Board for approval. The Regional Director acts as the secretary of the Regional Committee, which regularly meets in August (WHO Africa, 2024).

In 1992, the WHO Programme for International Drug Monitoring received reports of adverse reactions from its first African center (Isah *et al*., 2011).

2.6.1 Factors affecting ADR reporting in Africa

Despite recent efforts to harmonise PV regulations in Africa, low- and middle-income countries (LMIC) still face challenges with regards to development of robust PV systems which are capable of generating data which can be used to enlighten healthcare professionals and further improve healthcare policies and procedures (Kiguba *et al.*, 2023).

Some medicines' poor quality is a widespread and poorly acknowledged concern. Of 267 antimalarial medication samples in Cameroon, Ethiopia, Ghana, Kenya, Nigeria, and Tanzania, 76 (28%) were deemed unsatisfactory in a 2008 inspection. There were significant differences among countries, with Nigeria having the greatest failure rate (64%) and Ethiopia and Kenya having the lowest (0%) and 5%, respectively (Wirtz *et al*., 2016).

PV in Africa has changed over the past 10 years, particularly on the monitoring of new vaccines and treatments. However, less than 30% of African countries have robust PV systems meeting global standards. This is due to the lack of legal mandate on PV activities (Pharmaadmin, 2024).

2.6.2 The future ahead for Pharmacovigilance in Africa

50 to 54 countries in Africa are currently Participants in the WHO International Drug Monitoring Program. Despite PV development in Africa over the past few years, there are still challenges facing some countries in the African continent such as inadequate PV regulations, lack of adequate resources and political differences (Ndagije *et al.*, 2023).

The growing number, variety, and complexity of available treatments raises the risk of adverse events and makes it more difficult for healthcare professionals to accurately and reliably assess safety data. Artificial intelligence (AI) is being used in high-income nations to cope with the growing workload and the large amounts of safety data created as a result of scientific breakthroughs. In the same way, Africa is anticipated to prioritise AI in order to overcome certain barriers and ensure long-term patient safety results (Ndagije *et al*., 2023).

The road ahead for pharmacovigilance in Africa looks promising. Africa continues to strengthen PV systems and regional collaboration can also strengthen pharmacovigilance in Africa through shared benefits and harmonised regulations (Afri Summit, 2024).

2.7 South African Pharmacovigilance awareness

NADEMC, or the National Adverse Drug Event Monitoring Center, was founded in 1987. The South African Health Products Regulatory Authority (SAHPRA), which was founded to support with ADR monitoring, includes NADEMC as one of its units. The collecting and assessment of submitted ADR reports is managed by the NADEMC. In 1992, South Africa became the first African nation to join the WHO International Drug Monitoring Program (Mehta *et al*., 2017).

All medications registered in South Africa are subject to the pharmacovigilance regulations and best practices. The primary objective of the regulation is to improve patient safety and pharmacovigilance by strengthening and standardising it (www.sahpra.org.za, 2023).

In 2011, the National Department of Health (NDoH) program regional PV unit expanded TSR systems to include TB medications in addition to ARVs. HCPs received training as part of this program, and bulletins with updates on national PV initiatives were published (Rikhotso, 2021).

Three key stakeholders in South Africa are primarily responsible for driving PV initiatives: public health programs (which focus on systems); healthcare providers and clinicians (who focus on patients); and regulators and pharmaceutical companies (who focus on products) (Mehta *et al*., 2017).

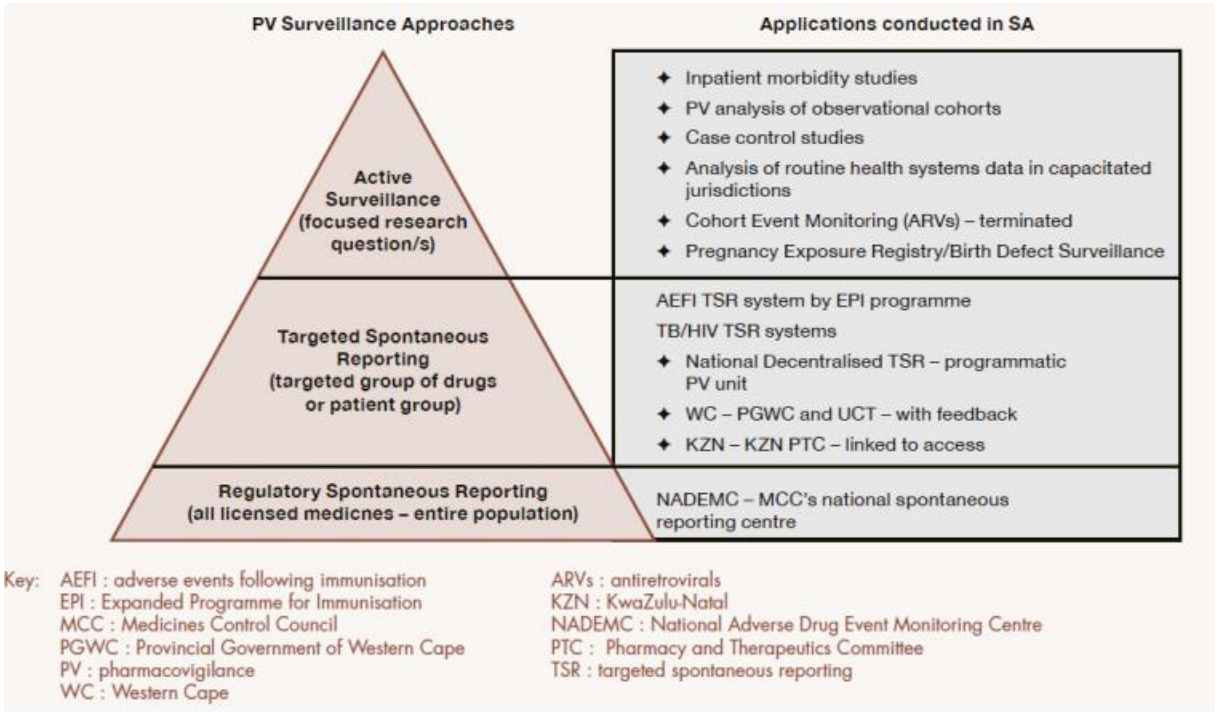


Figure 2.4 above illustrate pharmacovigilance approaches in South Africa (Rikhotso, 2021).

2.7.1 Factors affecting ADR reporting in SA

Research has been conducted to determine factors contributing to underreporting of ADRs in South Africa by healthcare professionals. A 2019 study by Haines *et al*. indicated that the major factors perceived to discourage ADR reporting are knowledge related such as not knowing how an ADR is reported, timelines for ADR reporting and where to send the ADR report (Haines et al., 2019). A study by Bogolubova et al highlighted that pharmacists feel discouraged to report ADRs as no feedback is received regarding reported ADRs (Bogolubova et al, 2018).

A study by Terblanche et al highlighted a concern of under reporting of ADRs by pharmacists in many countries including SA. This could be attributed to inadequate general knowledge towards PV as pharmacists in the research study confirmed they would like to receive training on ADR reporting (Terblanche et al., 2017). A research study by Gordhan and Bangalee identified time allocation for ADRs as the most common barrier to ADR reporting as stated by the majority of pharmacists' participants and felt not encouraged to report ADRs even if renumerated (Gordan and Bangalee, 2022).

Gordhon and Padayachee's 2020 research of doctors, nurses, and pharmacists found that lack of knowledge and time restrictions were two of the main variables influencing ADR reporting in South Africa. Above 80% of pharmacists and 54% of doctors were aware of how ADRs are but over 50% of nurses did not (Gordhon and Padayachee, 2020). According to the results of a research by Rikhotso, the most frequent explanation for failing to report ADRs is knowledge. This is despite the fact that just around half of the respondents had previously reported an adverse drug reaction (ADR), while over 81% of them indicated they had an ADR in patients (Rikhotso, 2021).

2.7.2 The future ahead for Pharmacovigilance in SA

PV in SA has a bright future. An initial three-year grant from the European Commission (through the EU Delegation in South Africa) is being used to support the development of a Center of Excellence (CoE) for Pharmacovigilance in Southern Africa (CEPSA) by the Western Cape University School of Pharmacy in collaboration with the Institute of Tropical Medicine, Antwerp, Belgium (ITM). The three main areas will be the CoE's focus:

- To assist a new generation of PV specialists and opinion leaders in Southern Africa, advanced training and capacity building are needed.
- Supporting pharmacovigilance operational research to optimise the creation and sharing of new local knowledge; and
- Improving information and communication platforms to provide prompt and interactive dialogue with communities and decision-makers regarding vaccine and medication safety (CEPSA, 2024).

PV operations in South Africa are shifting from relying on passive surveillance reporting to a more interactive approach that includes active monitoring with cohort studies, record-linkage projects, and the creation of patient registries, in line with global trends (Mehta *et a*l., 2017).

Chapter 3 Methods

3.1 Study Design

Qualified industrial pharmacists from South African pharmaceutical companies participated in this quantitative, cross-sectional study design. At the time of the approval of the research protocol, there were 276 active pharmaceutical license establishments in South Africa (www.sahpra.org.za, 2023).

Table 3.1: Active pharma licensed establishments in South Africa (SAHPRA website, 2023).

Active Pharma Licensed Establishments	Total Number
API Manufactures	8
API Importers and Exporters	1
Bond Stores	2
Gas Manufacturers	9
Importers and Exporters	175
Manufacturers and Packers	62
Testing Laboratories	19
Total	**276**

3.2 Study Setting

RedCaP online platform was utilised to capture all responses. This secure web-based platform is fast, safe, and easy for completion of research questionnaires.

3.2.1 Sample Size

Statistics as of July 25, 2023, indicated that there were 277 pharmacists working in manufacturing pharmacies in all nine provinces, according to the South African Pharmacy Council database. A sample size of 162 was calculated using a sample size calculator (Calculator.net):

Using a 95% confidence level, the calculator calculated the lowest number of samples needed based on the size of the entire population.

3.2.2 Source of Respondents

The South African Association of Pharmacists in Industry (SAAPI), Innovation Pharmaceutical Association South Africa (IPASA), and Southern African Pharmaceutical Regulatory Association (SAPPRA) are among the pharmaceutical

associations and retail pharmacies that were contacted to send the research questionnaire to their members via email. Only IPASA and SAPPRA accepted the request and both associations have representation of pharmacists with manufacturing experience. The sample reflected a wide range of company types and PV roles. IPASA comprises of numerous research-based pharmaceutical companies across SA with various working groups including PV, QA and Regulatory. SAPPRA is a society of professionals, largely pharmacists, involved in medicines regulation in South Africa. The majority of members work in the pharmaceutical industry or are pharmaceutical consultants.

3.2.3 Sample Selection

In South Africa, healthcare professionals such as nurses, physicians, and pharmacists are usually the ones that report adverse drug reactions (ADRs). According to earlier studies on healthcare professionals' knowledge, attitudes, and perceptions of pharmacovigilance, pharmacists play a major role in the underreporting of adverse drug reactions (ADRs) in South Africa and around the world. The target demographic for this study was pharmacists with prior experience in the pharmaceutical sector.

3.2.3.1 Inclusion Criteria

- Pharmacists above 18 years of age
- Pharmacists with Pharmaceutical manufacturing/industry experience of 1 year and above

3.2.3.2 Exclusion Criteria

- Non-pharmacists
- Pharmacists with no working experience in pharmaceutical manufacturing/industry.

3.3 Instrumentation and Outcome Measures

The questionnaire was developed based on similar research studies by other researchers, literature review of ADR requirements and guidance from this research supervisor (Gordhon and Padayachee, 2020; Joubert and Naidoo 2016; Rikhotso, 2021; Bogolubova *et al.*, 2018). The questionnaire comprised of four sections with a total of twenty-four questions based on similar studies; six questions about baseline demographics, eight about pharmacovigilance knowledge, five about attitudes using a

Likert scale that ranged from strongly disagree to strongly agree, three about how pharmacists perceived ADR reporting, and two about pharmacists' current pharmacovigilance practices.

3.3.1 Baseline demographics questions included: gender, age, position in pharmaceutical organisation, number of years working in pharmaceutical organisation, highest level of qualification, where undergraduate education was undertaken and previous training received on pharmacovigilance. The relationship between baseline demographics and knowledge, attitude, and perception scores and current practice was determined by using baseline demographic characteristics scores.

3.3.2 Section on background pharmacovigilance knowledge of the respondents comprised of eight questions. This included: pharmacovigilance definition, important purpose of pharmacovigilance, scope of ADR reporting inn South Africa, document/form to be used for ADR reporting, where ADRs are reported in South Africa, timelines for reporting ADRs, Medsafety knowledge and PSUR/PBRER definition. Data was used to determine knowledge level of each respondent towards pharmacovigilance, ADR reporting and ADR reporting process.

3.3.3 A Likert scale questions were used to measure and quantify attitudes, ranging from strongly disagree to strongly agree. Attitude towards pharmacovigilance was measured by five questions which included: reporting of ADR is considered an important activity to ensure safety of medicines, consulting colleagues and other healthcare professionals is important before reporting an ADR, educational background has provided enough information about ADR reporting, ADR reporting is an obligation in roles in pharmaceutical organisation and there is adequate awareness regarding pharmacovigilance. Data was used to determine general attitude by respondents towards pharmacovigilance and ADR reporting and also potentially identify factors that contribute to under reporting of ADRs in South Africa.

3.3.4 Three perception questions included:

- If it is perceived easy to complete ADR reporting form by respondents.
- If the current system of reporting ADRs is perceived to be efficient.
- Perception on education towards improvement of managements of ADRs in South Africa.

Perception was explored by analysing quantitative data from close-ended questions to identify recurring themes and patterns in perceptions.

3.3.5 Two questions focused on current practices of pharmacists regarding the ADR reporting framework in South Africa:

- The first question was on whether respondents have had to complete an ADR reporting form.
- Second question was on whether respondents have been required to submit an ADR report to SAHPRA.

Data was used to gain knowledge on the current practices of ADR reporting by pharmacists in South Africa to identify any areas of improvement.

3.4 Procedure

3.41 Pilot Study

The questionnaire was validated by two (2) experts prior to piloting it. The first expert was a senior lecturer in the faculty of health sciences, Department of Pharmacy at the University of Limpopo. The expert was a PhD graduate and an honorary research fellow from the University of Kwazulu-Natal with more than eighteen research publications in various health sciences disciplines. The second expert is a lecturer in the faculty of health sciences, Department of Pharmacy and pharmacology at the University of Witwatersrand. The expert holds an MPharm degree and is a PhD candidate with more than seven research publications.

A 2002 study by Van Teijlingen identified that one benefit of carrying out a pilot study is that it may provide early warning about potential failure points for the main research project, possible breaches of research protocols, and whether suggested instruments or methodologies are unsuitable or overly complex (Van Teijlingen, 2002). The experts were asked about their interpretations of the questionnaire's questions, whether they were clear enough to prevent misunderstandings, whether the format was easy to use, and whether the quantity and length of the questions encouraged respondents to complete it. The experts were also asked to suggest any additional questions that should be included in the questionnaire and to specify how long it ought to take to complete. The questionnaire was amended based on the feedback received from the two (2) experts prior to pilot study. The estimated time that the study would take was

approximately 10 – 15 minutes. This was particularly expected given that multiple choice questions (MCQ) type questions typically take time to discern between available choices.

Thereafter, the questionnaire was then piloted by twelve (12) selected pharmacists in scope of the target population. Anonymity and confidentiality of the pilot respondents' feedback was assured. These respondents were included in the larger study.

3.4.2 Main Study

Bulk e-mail was sent out by Innovation Pharmaceutical Association South Africa (IPASA) and South African Pharmaceutical Regulatory Association (SAPRAA) to their members requesting them for their participations towards this research study.

The e-mail included a RedCap online survey link which takes the respondent to the questionnaire. Other social platforms such is LinkedIn were also used for distribution of the RedCap online survey link to target respondents. The respondents were assured of confidentiality and anonymity.

3.5 Ethical Considerations

Ethics clearance to conduct this research study was obtained from the University of the Witwatersrand Human Research Ethics Committee (Non-Medical) (R14/49 clearance certificate number: H23/09/26).

RedCaP online survey platform was utilised for this research study. A respondent information sheet where respondents were informed of the voluntary participation was included on first page of the online research questionnaire. Participation information sheet included the following: research study was confidential and anonymous; if the respondents decided to take part in this research study, it should be because they wanted to volunteer; respondents do not have to answer any questions if they do not want to; they will not receive any direct benefits if they choose to participate; they will not lose any services, benefits, or rights they would typically have if they choose not to participate; participating in this study will not cost them anything; they will not receive payment for their participation; and completing and submitting the online survey is interpreted as consent to participate.

3.6 Data reduction and Statistical Analyses

Participation the questionnaire occurred over a period between April 2024 and February 2025 in which data was captured directly in RedCap online platform. Only the researcher had access to the questionnaire responses. Each completed questionnaire record was assigned with a unique record identification number. For simplicity during analysis, each variable category was coded with numerical values. Satisfy software was used to calculate descriptive statistical analysis. Mean, range, median and standard deviation was calculated for the demographic variables. Results were presented by means of percentage, tables and graphs depending on the appropriateness of the variable in question. The relationship between demographic variables (e.g. age, numbers of years working at pharmaceutical organisation, etc) versus knowledge, attitude and perception variables was determined using the Chi-Square to analyse the responses. Frequency analysis was also calculated to establish differences in knowledge, attitudes, perception and current practices.

Chapter 4 Results

A total of 85 responses were received within a period of 9 months providing a sample response rate of 52.5%.

4.1 Baseline Demographics

The majority of the respondents were female (59, 69.4%) compared to (26, 30.6%) who were male. The highest number of respondents were between the ages of 25 and 34 years (30, 35.3%) followed by the 35 – 44 years (23, 27.1%) age band, Table 4.1.

The highest number of respondents held a position in Regulatory Affairs department in the pharmaceutical organisation (33, 38.8%). More than 20% of the respondents selected 'other' for the position in the pharmaceutical organisation as an indication that the position in the pharmaceutical organisation is not in regulatory affairs, quality assurance, pharmacovigilance or production (19, 22.9%).

The highest number of respondents have been working in the pharmaceutical organisation for 1 – 5 years (24, 28.2%) and most of the respondents have a Bachelor of Pharmacy (B.Pharm) (59, 69.4%) as the highest level of education.

The majority of the respondents completed their undergraduate education at local universities (62, 72.9%). Most of the respondents confirmed having received in-house training on management of ADRs previously (53, 62.4%) however; over 15% of the respondents have no additional PV training other than undergraduate training has been undertaken (13, 15.3%).

For demographic data, the mean value was calculated to perform measures of trend analysis, and the standard deviation was calculated to determine measures of variability, Table 4.1. Std. deviation values of gender, highest level of education and previous training received baseline demographic characteristics were less than one indicating that the data points are generally close to the mean. The low std. deviation implied that there was less variability and data was consistent. In contrast, std. deviation values for age of respondents, position of respondents and number of years working in pharmaceutical organisation baseline demographic characteristics were higher than one indicating that the data points are generally not close to the mean which signifies a higher level of variability.

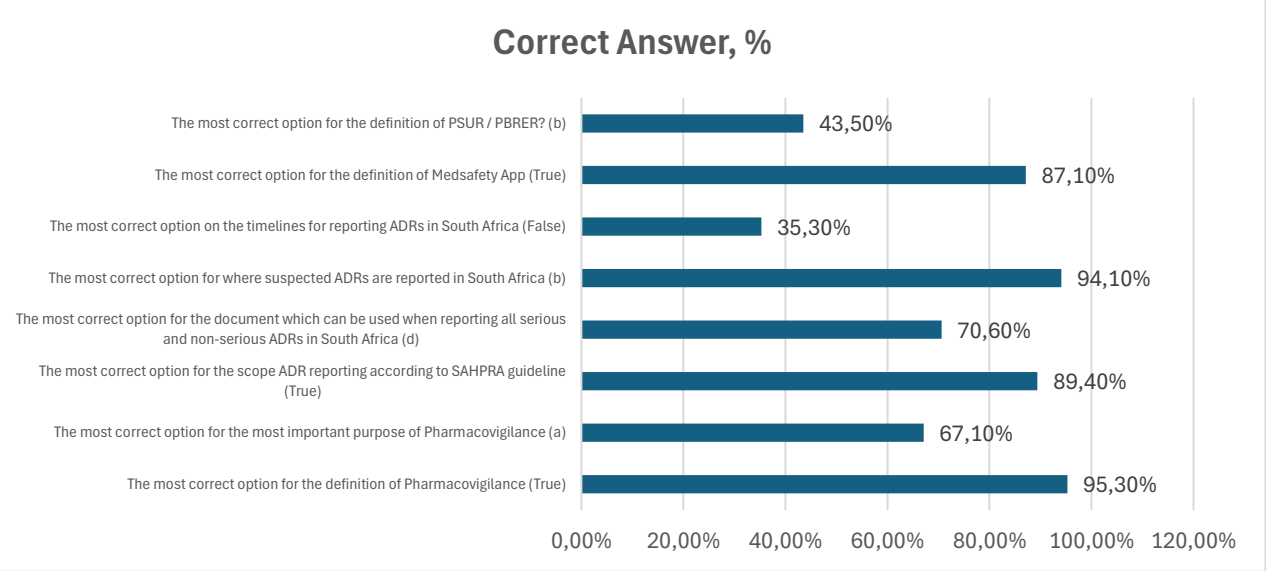
Table 4.1: Baseline demographic characteristics.

Baseline demographic characteristic	**Frequency (*n*)**	**Percentage (%)**
Gender of respondent, n (%)		
Female	59	69.4
Male	26	30.6%
Total	**85**	**100.0**
Mean	**1.31**	
Std. Deviation	**0.46**	
Age of respondent, n (%)		
18 - 24	2	2.4
25 - 34	30	35.3
35 - 44	23	27.1
45 - 54	19	22.4
Above 54	11	12.9
Total	**85**	**100.0**
Mean	**3.08**	
Std. Deviation	**1.09**	
Position in the pharmaceutical organization, n (%)		
Regulatory Affairs	33	38.8
Quality assurance	20	23.5
Pharmacovigilance	6	7.1
Production	6	7.1
Other	19	22.9
Unspecified	1	1.2
Total	**85**	**100.0**
Mean	**2.54**	
Std. Deviation	**1.62**	
Position in the pharmaceutical organization if other was selected on question above, n (%)		
Clinical Operations	3	3.5
Pharmaceutical Depot	1	1.2
Medical Affairs	2	2.4
Responsible Pharmacist	3	3.5
Retail Pharmacy	6	7.1
Health Policy and General Operations	3	3.5
Unspecified	1	1.2
Total	**19**	**22.4**

Number of years working in the pharmaceutical organization, n (%)		
1 – 5 years	24	28.2
6 – 10 years	19	22.4
11 – 20 years	23	27.1
>20 years	17	20.0
Unspecified	2	2.4
Total	**85**	**100.0**
Mean	**2.63**	
Std. Deviation	**1.91**	
Highest level of education, n (%)		
Bachelor of Pharmacy (B.Pharm)	59	69.4
Master of Pharmacy (M.Pharm)	16	18.8
Doctor of Philosophy in various fields of Pharmacy and Pharmacology	2	2.4
Unspecified	8	9.4
Total	**85**	**100.0**
Mean	**1.26**	
Std. Deviation	**0.5**	
Where undergraduate education was undertaken, n (%)		
South Africa	62	72.9
Outside of South Africa	1	1.2
Unspecified	22	25.9
Total	**85**	**100.0**
Previous training received on pharmacovigilance, n (%)		
In-house training on management of ADRs	53	62.4
Pharmacovigilance training offered by recognized associations such as SAAPI, SAHPRA, etc.	15	17.6
No additional PV training other than undergraduate training has been undertaken	13	15.3
Unspecified	4	4.7
Total	**85**	**100.0**
Mean	**1.57**	
Std. Deviation	**0.84**	

4.2 Knowledge questions pertaining to Pharmacovigilance

Figure 4.1: Frequency distribution of respondents' knowledge.



Most respondents were aware of the definition of pharmacovigilance (81, 95.3%) while 94% knew where to report ADRs (80, 94.1%). The lowest scores were obtained on timelines for reporting serious ADRs in South Africa (30, 35.3%) and on what the definition for PSUR/PBRER are (37, 43.5%).

Relationship between respondents' demographic characteristic and knowledge scores was determined by inferential analysis using the Chi-Square, Table 4.2.
There was a strong significance of position and education level with knowledge. It shows that people in position quality assurance and people with M.Pharm level of education have better pharmaceutical knowledge.

Descriptive analysis of correct responses by years of experience in the pharmaceutical organization revealed that individuals with 1–5 years and 11–20 years of experience demonstrated higher levels of pharmacovigilance knowledge compared to other groups. This may reflect a combination of recent academic exposure and accumulated practical experience. However, those with over 20 years of experience showed moderate knowledge levels, while the group with unspecified years of service had the lowest number of correct responses.

The majority of correct responses were concentrated among those holding a Bachelor of Pharmacy (B.Pharm) degree. Respondents with M.Pharm or PhD degrees exhibited

notably fewer correct responses, which may be attributed to specialisation in non-pharmacovigilance-related fields or reduced exposure to routine PV reporting practices. These findings suggest that practical, undergraduate-level exposure to pharmacovigilance concepts may play a more critical role in knowledge retention and application than postgraduate qualifications.

Respondents who had received in-house ADR management training performed the best, especially on questions related to the definition and scope of pharmacovigilance. In contrast, individuals with no additional PV training beyond their undergraduate education showed the lowest levels of correct responses. These findings underscore the importance of practical, in-house training for enhancing knowledge and ensuring effective pharmacovigilance practices.

Table 4.2 Correlation between knowledge and demographic characteristics.

	PV definition	Purpose of PV	Scope of ADR reporting	Form used for ADR reporting	Where ADRS are reported	Timelines for ADR reporting	Medsafety definition	PSUR/PBRER definition	P value by Chi-Square
Age of respondent									
18 - 24 years n (%)	2 (2.4)	2 (2.4)	2 (2.4)	1 (1.2)	2 (2.4)	0 (0.0)	2 (2.4)	0 (0.0)	0.1416
25 - 34 years n (%)	26 (30.6)	20 (23.5)	28 (32.9)	20 (23.5)	28 (32.9)	12 (14.1)	26 (30.6)	12 (14.1)	0.5081
35 - 44 years n (%)	23 (27.1)	15 (17.6)	20 (23.5)	17 (20.0)	22 (25.9)	6 (7.1)	21 (24.7)	10 (11.8)	0.4413
45 - 54 years n (%)	19 (22.4)	13 (15.3)	15 (17.6)	14 (16.5)	19 (22.4)	8 (9.4)	16 (18.8)	10 (11.8)	0.3984
Above 54 years n (%)	11 (12.9)	7 (8.2)	11 (12.9)	8 (9.4)	9 (10.6)	4 (4.7)	9 (10.6)	5 (5.6)	0.5435
Position in the pharmaceutical organization									
RA n (%)	29 (34.1)	20 (23.5)	30 (35.3)	23 (27.1)	31 (36.5)	17 (20.0)	27 (31.8)	13 (15.3)	0.1536
QA n (%)	19 (22.4)	16 (18.8)	19 (22.4)	14 (16.5)	17 (20.0)	3 (3.5)	18 (21.2)	5 (5.9)	**0.0447**
PV n (%)	6 (7.1)	5 (5.9)	4 (4.7)	5 (5.9)	6 (7.1)	3 (3.5)	5 (5.9)	4 (4.7)	0.2423
Production n (%)	6 (7.1)	4 (4.7)	5 (5.9)	5 (5.9)	6 (7.1)	0 (0.0)	6 (7.1)	3 (3.5)	0.1169
Other n (%)	19 (22.4)	11 (12.9)	17 (20.0)	12 (14.1)	19 (22.4)	7 (8.2)	17 (20.0)	11 (12.9)	0.2998
Unspecified n (%)	1 (1.2)	1 (1.2)	1 (1.2)	1 (1.2)	1 (1.2)	0 (0.0)	1 (1.2)	1 (1.2)	0.3274

Number of years working in the pharmaceutical organization									
1 - 5 years n (%)	23 (27.1)	14 (16.5)	23 (27.1)	15 (17.6)	24 (28.2)	8 (9.4)	22 (25.8)	10 (11.8)	0.4270
6 - 10 years n (%)	16 (18.8)	14 (16.5)	16 (18.8)	13 (15.3)	17 (20.0)	7 (8.2)	16 (18.8)	7 (8.2)	0.5086
11 - 20 years n (%)	22 (25.9)	17 (20.0)	19 (22.4)	17 (20.0)	22 (25.9)	6 (7.1)	21 (24.7)	9 (10.6)	0.3623
>20 years n (%)	17 (20.0)	10 (11.8)	16 (18.8)	13 (15.3)	15 (17.6)	7 (8.2)	14 (16.5)	8 (9.4)	0.4645
Unspecified n (%)	2 (2.4)	2 (2.4)	2 (2.4)	1 (1.2)	2 (2.4)	1 (1.2)	1 (1.2)	2 (2.4)	0.1657
Highest level of education									
B.Pharm n (%)	57 (67.1)	42 (49.4)	53 (62.4)	42 (49.4)	56 (65.9)	16 (18.8)	53 (62.4)	21 (24.7)	0.2398
M.Pharm n (%)	14 (16.5)	10 (11.8)	14 (16.5)	11 (12.9)	15 (17.6)	10 (11.8)	14 (16.5)	11 (12.9)	**0.0458**
PhD n (%)	2 (2.4)	1 (1.2)	2 (2.4)	1 (1.2)	2 (2.4)	2 (2.4)	2 (2.4)	1 (1.2)	0.1442
Unspecified n (%)	7 (8.2)	4 (4.7)	7 (8.2)	6 (7.1)	7 (8.2)	2 (2.4)	5 (5.9)	4 (4.7)	0.3422
Previous training received on pharmacovigilance									
In-house training n (%)	51 (60.0)	39 (45.9)	51 (60.0)	41 (48.2)	49 (57.6)	19 (22.4)	47 (55.3)	21 (24.7)	0.4641
No additional PV training n (%)	13 (15.3)	6 (7.1)	11 (12.9)	7 (8.2)	13 (15.3)	2 (2.4)	12 (14.1)	6 (7.1)	0.1128

PV training offered by recognized associations n (%)	14 (16.5)	10 (11.8)	12 (14.1)	10 (11.8)	15 (17.6)	7 (8.2)	14 (16.5)	7 (8.2)	0.4011
Unspecified n (%)	2 (2.4)	2 (2.4)	2 (2.4)	1 (1.2)	2 (2.4)	1 (1.2)	1 (1.2)	2 (2.4)	0.1657

4.3 Attitudes and perceptions toward ADR reporting

The responses in Table 4.3 indicate a generally positive attitude towards ADR reporting among healthcare professionals, with 98.8% agreeing on its importance for drug safety. However, there were mixed responses regarding consulting colleagues before reporting an ADR, with 50.6% agreeing it is important, but a significant 27.1% disagreeing, reflecting varied practices. The majority of respondents felt they were obligated to be involved in ADR reporting (94.1%), indicating strong commitment to pharmacovigilance. However, concerns about educational gaps remain, with 25.9% disagreeing that their educational background provides sufficient information for ADR reporting. Furthermore, while 60% feel there is adequate awareness of PV in their environments, 20% disagreed, suggesting that further awareness initiatives might be necessary

Table 4.3 Attitudes and perceptions towards ADR reporting.

#	Question	Agree, n (%)	Neither agree nor disagree, n (%)	Disagree, n (%)
1	Reporting of adverse drug reactions is an important activity to ensure safety of medicines	84 (98.8%)	1(1.2%)	0 (0.0%)
2	Consulting colleagues and other healthcare professionals is important before reporting an ADR	43 (50.6%)	18 (21.2%)	23 (27.1%)
3	Educational background has provided me with enough information about ADR reporting	46 (54.1%)	16 (18.8%)	22 (25.9%)
4	I am obligated to be involved in ADR reporting in my role in the organisation	80 (94.1%)	4 (4.7%)	1 (1.2%)
5	There's adequate awareness regarding pharmacovigilance in your professional environment	51 (60.0%)	16 (18.8%)	17 (20.0%)

Responses towards attitude and perception on how easy it is to fill in ADR reporting form are included in Table 4.4. Many respondents (52.9%) found completing the ADR reporting form to be "easy," with 29.4% indicating that it was "slightly difficult." A smaller percentage (7.1%) considered it "difficult" or "very easy.

Table 4.4: Attitudes and perceptions towards ADR reporting.

#	Question	Difficult, n (%)	Slightly difficult, n (%)	Easy, n (%)	Very easy, n (%)
6	How easy it is to complete/fill in ADR reporting form?	6 (7.1%)	25 (29.4%)	45 (52.9%)	6 (7.1%)

Above 40% perceived the system as "slightly efficient," with 40.0% rating it as "moderately efficient." A smaller percentage (12.9%) felt that the current system is "not efficient, Table 4.5.

Table 4.5: Attitudes and perceptions towards ADR reporting.

#	Question	Not efficient, n (%)	Slightly efficient, n (%)	Moderately efficient, n (%)
7	How efficient is the current system of reporting ADRs?	11 (12.9%)	40 (47.1%)	34 (40.0%)

More than half (56.5%) believe that education through PV conferences would be the most effective way to improve ADR management, followed by 24.7% supporting increased supervision of junior pharmacists. A smaller percentage (18.8%) felt that discussing solutions with other pharmacists would be key, Table 4.6.

Table 4.6: Attitudes and perceptions towards ADR reporting.

#	Question	Discussing solutions with other pharmacists, n (%)	Education through PV conferences, n (%)	Increased supervision of junior pharmacists to ensure that ADRs are managed correctly, n (%)
8	Which of the following should be implemented to improve management of ADRs?	16 (18.8%)	48 (56.5%)	21 (24.7%)

Tables 4.7 and 4.8. shows significant correlations between age and position in the pharmaceutical organization.

The number of years working in the pharmaceutical organization showed significant results for some of the questions related to ADR reporting and education.
Educational background and previous training received on PV showed mixed results, with some areas being significant while others were not.

Table 4.7: Correlation of baseline demographic characteristics with attitude and perception responses towards ADR reporting.

	Reporting of adverse drug reactions is an important activity to ensure safety of medicines **(P value by Chi-Square)**	**Consulting colleagues and other healthcare professionals is important before reporting an ADR** **(P value by Chi-Square)**	**Educational background has provided me with enough information about ADR reporting** **(P value by Chi-Square)**	**I am obligated to be involved in ADR reporting in my role in the organisation** **(P value by Chi-Square)**	**There's adequate awareness regarding pharmacovigilance in your professional environment** **(P value by Chi-Square)**
Gender of respondent	0.0970	0.0681	0.1897	0.1100	0.1100 .
Age of respondent	**0.0000**	**0.0000**	**0.0000**	**0.0357**	**0.0098**
Position in the pharmaceutical organization	**0.0001**	**0.0000**	**0.0001**	**0.0000**	**0.0000**
Number of years working in the pharmaceutical organization	0.0792	**0.0001**	**0.0000**	**0.0021**	**0.0000**
Highest level of education	0.4641	**0.0001**	**0.0001**	0.1286	**0.0002**
Previous training received on pharmacovigilance	0.3922	**0.0000**	**0.0001**	0.0129	**0.0000**

Table 4.8: Correlation of baseline demographic characteristics with attitude and perception responses towards ADR reporting.

	How easy it is to complete/fill in ADR reporting form? **(P value by Chi-Square)**	**How efficient is the current system of reporting ADRs?** **(P value by Chi-Square)**	**Which of the following should be implemented to improve management of ADRs?** **(P value by Chi-Square)**
Gender of respondent	0.1074	0.0545	0.7123
Age of respondent	**0.0096**	**0.0002**	**0.0005**
Position in the pharmaceutical organisation	**0.0001**	**0.0001**	**0.0005**
Number of years working in the pharmaceutical organisation	**0.0000**	**0.0001**	**0.0000**
Highest level of education	**0.0001**	**0.0007**	**0.0008**
Previous training received on pharmacovigilance	**0.0010**	**0.0000**	**0.0010**

Age, position in the pharmaceutical organization, number of years working in the pharmaceutical organization, highest level of education, and previous training received on pharmacovigilance showed significant results across all three areas: ease of completing the ADR form, efficiency of the reporting system, and proposed solutions for improving ADR management. However, gender of respondent was not significantly correlated with any of the areas.

4.4 Current practices of pharmacists regarding the ADR reporting framework in SA

The majority of respondents did not complete an ADR form or submit an ADR form to SAHPRA, Table 4.9.

Table 4.9: ADR reporting form and submission of ADR report to SAHPRA.

#	Question	I have completed an ADR form, n (%)	I have never completed an ADR form, n (%)
1	Have you had to complete an ADR reporting form?	33 (38.8%)	50 (58.8%)
		I have submitted an ADR report to SAHPRA, n (%)	**I have never submitted an ADR report to SAHPRA, n (%)**
2	Have you been required to submit an ADR report to SAHPRA?	20 (23.5%)	63 (74.1%)

Chapter 5 Discussion

5.1 Introduction

This chapter discusses the results achieved from this research study. The achieved results were compared to other results in similar studies to highlight similarities and any noted differences. Recommendations for future research studies, strengths and limitations identified as part of this research study will be discussed.

5.1.1 Baseline Demographics

The targeted sample population for this research study was limited to pharmacists in pharmaceutical organisation. A total of 85 complete surveys were received, which was a 52.5% response rate. This response rate is not far off from the response rates achieved in similar studies. The 52.5% is higher than the response rate achieved in a similar study by Gordhan and Bangalee. (Gordan and Bangalee, 2022). However, the 52.5% response rate was lower but comparable to those attained in a study by Alam *et al*. in Dharan which was 58.3% (Alam *et al.,* 2021), and KAP study of nurses and pharmacists towards adverse drug reaction reporting in the SA which was 52.59% (Bogolubova *et al*., 2018)

In general, online survey often see lower response rate compared to in-person surveys. Based on Customer Thermometer, survey response rates in the 5% to 30% range are far more typical. A survey response rate of 50% or higher should be considered excellent in most circumstances (Customer Thermometer, 2024).

About 70% of the respondents were females. The high number of female respondents is expected as generally pharmacy is a female dominated profession. There are over seventeen thousand registered pharmacists in SA and almost two-thirds of those are females (FIP, 2024). Pharmacists' demographics and statistics in the United States confirmed that about 57% of all pharmacists are females (ZIPPIA, 2025).

Most of the pharmacists in SA are younger than 55 years with most falling below the age of 35 years (sapc website - SAPC, 2011). This distribution of pharmacists by age analysis is aligned with the findings in this research study which was in the age band of between 25 and 34 years. This was similarly reported in other studies (Bharathi *et al*., 2022; Alam *et al.,* 2021). The majority of the respondents in this research study were in regulatory affairs roles which was expected as a pharmacy qualification is one of the prerequisites in order to assume a role in regulators affairs.

More than 20% of the respondents in this research study had between 11 and 20 years of experience in pharmaceutical organisation. The high number of respondents with more than 10 years of experience is consistent with the findings in the 2018 KAP study by Bogolubova *et al.* where the majority of the respondents had more than 10 years of experience as a healthcare professional (Bogolubova *et al*., 2018).

Over 60% of the respondents in this research study confirmed that they had in house training on management of ADRs. This was a positive response; however, this baseline demographic also highlighted the 15% of the respondents which had no additional PV training other than undergraduate training undertaken. A 2017 study on evaluation of knowledge and perceptions about PV activities among pharmacy students in Nigeria confirmed similar findings where over seventy-five respondents indicated that they have completed a PV course with about 20% indicating that they have not completed a PV course (Olubunmi and Patrick 2017).

5.2 Knowledge pertaining to Pharmacovigilance

Over 95% of the respondents have adequate knowledge of PV definition. The positive results can be attributed to the PV training previously received as a total of about 80% of respondents indicated that they have received either in-house training on management of ADRs (53, 62.4%) or PV training offered by recognized associations (15, 17.6%). The mean knowledge score achieved in this research study was about 70% (85, 72.8%). The knowledge results corroborate with the findings of previous studies conducted elsewhere (Gordhan and Bangalee, 2022; Joubert and Naidoo, 2015; Gordhon and Padayachee, 2020; Alam *et al*., 2021; Atia *et al.*, 2021; Olubunmi and Patrick, 2017; Alwhaibi and Aloola, 2020; Tahir and Hussein, 2020; Bogolubova et al., 2018; Li *et al*., 2018; Shambhavi *et al*., 2023).

The age of the respondents, role of the respondents in the pharmaceutical organisation, the number of years of experience and previously received PV training influenced the knowledge scores in this research study.

The majority of the respondents did not have adequate knowledge of PSUR/PBER. This could be attributed to the insufficient details of PSUR/PBER in house-training content which most of the respondents have completed. Most of the respondents have knowledge of where ADRs are to be reported; however, the majority of the respondents are not aware of the timelines for reporting serious ADRs. ADR reporting awareness

seminars will provide a good opportunity for pharmacists to have better insights on PSUR/PBER and ADR reporting timelines.

Over 70% of the respondents are aware of the ADR form to use when reporting all serious and non-serious ADRs. This finding was consistent with the findings in other studies (Gordhon and Padayachee, 2020; Li *et al*., 2018).

5.3 Attitudes and perceptions toward ADR reporting

Most respondents agreed that reporting of adverse drug reactions is an important activity to ensure safety of medicines (84, 98.8%) while over 90% of the respondents agreed that they are obligated to be involved in ADR reporting in their role in the organisation (80, 94.1%). A similar KAP study by Rikhotso reported that the majority of respondents agreed that reporting of adverse drug reactions is necessary (Rikhotso, 2021), while a study by Joubert and Naidoo, the majority of respondents considered PV was a useful tool (Joubert and Naidoo, 2015). Additionally, pharmacists, in a study by Elbakay et al, expressed more positive attitudes regarding PV than did members of other healthcare professions, with the majority indicating that it was their responsibility to report ADRs (Elbakay *et al.,* 2023).

The positive attitude towards PV is encouraging as it indicates that the importance of ADR reporting in South Africa is well understood by healthcare professionals in particular, pharmacists.

Over 50% of the respondents in this research study agreed that consulting colleagues and other healthcare professionals is important before reporting an ADR with just over 50% of the respondents agreed that educational background has provided them with enough information about ADR reporting. This is an indication that PV training is not adequate as pharmacists are not provided with adequate knowledge and confidence to report ADRs. These results are similar to a 2021 study which indicated that awareness regarding PV in professional environments is inadequate (Rikhotso, 2021). Most of the respondents agreed that it is their obligation to be involved in ADR reporting in their role in the pharmaceutical organisation. This was an encouraging response which was corroborated by Alam *et al*. in a 2021 study where a majority of the pharmacists agreed that it is their responsibility to report ADRs (Alam *et al*., 2021) and a 2020 KAP study of community pharmacists towards PV and ADRs by Tahir and Hussein where the majority of the respondents indicated that it is their professional obligation to report ADRs (Tahir and Hussein, 2020).

About 47% of respondents agree that the system for reporting ADRs is only somewhat efficient, while more than 50% of respondents in this study found it easy to fill out the ADR reporting form. These results are consistent with a study on community pharmacists' knowledge, attitudes, perceptions, and practices regarding pharmacovigilance in Gauteng, South Africa, which found that most pharmacists would prefer an electronic reporting platform over a telephone, email, or facsimile system (Gordan and Bangalee, 2022).

5.4 Current practices of pharmacists regarding the ADR reporting framework in South Africa

Over 58% of the respondents in this research study have never completed an ADR form and about 57% of the respondents have never submitted an ADR report to SAHPRA. These findings could be attributed to the following:

- General inadequate knowledge level towards ADR reporting as most of the respondents confirmed that education through PV conferences should be implemented in order to improve management of ADRs in SA.
- Inadequate educational background as just 50% of the respondents agreed that educational background has provided them with enough information about ADR reporting.
- ADR form not easy and encouraging enough for ADRs to be reported, this was confirmed by about 50% of the respondents who do not find it easy to fill out ADR reporting forms.

These findings are in line with findings from similar studies. A 2024 study by Shambhavi *et al*. on assessment of KAP towards pharmacovigilance among pharmacists indicated that ADR reporting among pharmacists was poor (Shambhavi *et al*., 2024) and a 2025 study on KAP of PV amidst healthcare providers concluding indicating a low number of ADR reporting by pharmacists (Dey *et al*., 2025).

5.5 Improvements to the existing ADR reporting framework in South Africa

The research study questionnaire included a request for respondents to add any further improvements as applicable to the existing ADR reporting framework in South Africa. The top suggestions from the respondents included increased

pharmacovigilance awareness, regular webinars of pharmacovigilance to educate pharmacists to be considered by SAHPRA, regular updates and refresher workshops for healthcare professionals to be kept updated and digital forms with easy to populate fields instead of pdf forms to be considered. Other suggestions included financial incentives for consistent ADR reporting and patient consumer awareness. Similar recommendations were also made in a study by Gordan and Bangalee, which indicated that in order to improve, support, and promote ADR reporting, continuous ADR training and communication strengthening are necessary to further develop ADR understanding and reporting procedures (Gordan and Bangalee, 2022).

Chapter 6 Conclusion and Recommendations

6.1 Conclusion

The aim of this research was to identify and describe the knowledge, attitudes and perceptions of PV among pharmacists in pharmaceutical companies in SA.

Although above 95% of respondents in this research study have adequate knowledge of the definition of PV, there is still insufficient understanding on the importance of PV in medicine safety. A low number of respondents are aware of the timelines for reporting suspected ADRs in South Africa and the low correct response rate was also noted on the PSUR/PBRER knowledge. These findings highlight that perhaps more ongoing training needs to be conducted amongst pharmacists in the pharmaceutical industry but also the need to emphasise the importance of PV at undergraduate training level.

In conclusion, this research study supports the findings of other similar studies which suggests that lack of knowledge significantly contributes to the under reporting of ADRs by pharmacists in pharmaceutical organisation in South Africa.

6.2 Clinical/Practical Recommendations

6.2.1 Pharmacovigilance awareness campaigns and webinars

Pharmacovigilance in South Africa is evolving. There has been a lot of initiatives implemented to promote ADR reporting by both members of the public and healthcare professionals. This research study highlighted the need for more awareness webinars for pharmacists. This was also suggested by Matlala *et al.* on ADR reports submitted in South Africa based on VigiBase analysis for the year 2017, the study concluded that pharmacist reported the lowest number of cases. The low number of cases reported by pharmacists suggested that awareness on ADR reporting amongst pharmacist could enhance reporting rate in South Africa (Matlala *et al.,* 2017).

Gordan and Bangalee provided similar recommendations where the research study concluded that there was inadequate awareness of ADR reporting procedures. Poor ADR knowledge, low confidence, avoiding tasks that are seen as additional work, and a lack of awareness of ADR reporting procedures were also cited as reasons for the underreporting of ADRs. In order to increase, support, and promote ADR reporting, the

study also found that continuous ADR training and communication are necessary to strengthen ADR skills and reporting practices (Gordan and Bangalee, 2022).

Awareness campaigns can be in a form of social media updates on pharmacovigilance related topics. Pharmacovigilance online events will be of great benefit as face-to-face events are not always possible for healthcare professionals to attend from all corners of South Africa.

6.2.2 Development of electronic forms (e-forms), telephonic and e-mail reporting

As we evolve into the technological era, ADR reporting platforms need to follow suit. SAHPRA launched Medsafety App for self-reporting of suspected ADRs by the public and healthcare professionals. The introduction of SAHPRA Medsafety App in 2021 is one of the recent pharmacovigilance initiatives in South Africa. The App has great benefits including facilitating simple and convenient reporting of ADRs by the public and healthcare professionals. It also provides a readily platform to reporters for feedback about their submitted report. The App however has some limitations as it is currently only available in English (www.sahpra.org.za, 2021).

The Medsafety App requires a smart phone to be able to download the app. This is a downfall as not every member of the public and/or healthcare professional has a smart phone. Introduction of a digital real time platform with easy to populate digital ADR fields instead of current pdf forms can improve ADR reporting in South Africa. Digital real time platform introductions also come with challenge as not all healthcare facilities particularly in rural developments are equipped with computers. The digital platform recommendation should have a backup system in a form of simplified ADR forms which are easy to fill and effective. Minimum quantity of the simplified forms to be kept at each healthcare facility and pharmaceutical organisations.

6.3 Recommendation for Future Research

It is suggested that more research be done with a greater sample size, encompassing patients and other medical professionals who are qualified to report adverse drug reactions in South Africa. Future research to consider the following recommendations:

6.3.1 SAHPRA recommendations

The research study to investigate the effectiveness of Medsafety App used for ADR reporting, identify any barriers associated with the use of the APP and how those barriers can be mitigated. Introduction of ADR reporting e-forms to be considered and evaluate if e-forms encourages ADR reporting by pharmacists.

6.3.2 Pharmaceutical companies' recommendation

Future research studies to evaluate if renumeration can be a motivator to address under reporting of ADRs by pharmacists in pharmaceutical companies in South Africa.

6.3.3 Pharmacy education recommendation

Evaluate if undergraduate programmes in pharmacy offer sufficient PV training and if the training offered provides satisfactory self-confidence for pharmacists to report ADRs spontaneously.

6.4 Strengths and Limitations

The major strength of this research study was on the quality of the responses received from the 85 respondents. The responses required little data clean up to remove errors before moving to statistical analysis. While the limitation was the poor response rate, a study with a larger population size would provide richer results.

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Appendix

Appendix A: Information Sheet

Dear Sir / Madam

My name is Nkhumeleni Motsage. I am a Masters student in Medicine (Pharmaceutical Affairs) at the University of the Witwatersrand, Johannesburg. My supervisor is Dr Neelaveni Padayachee. I am conducting a research study about knowledge, attitudes, and perceptions of pharmacovigilance among pharmacists in pharmaceutical companies in South Africa.

I am inviting you to take part in a questionnaire. If you decide to take part, your participation in this research study will last about 5 minutes.

After completion of the questionnaire, pdf copies are saved. The pdf copied will be stored in password protected computer for 5 years. Only the researcher will have access to the data.

The research study will be confidential and anonymous. Your name or anything else that could identify you will not be required in this research study.

If you decide to take part in the research study, it should be because you want to volunteer. You do not have to take part. You can stop being in the study at any time. You do not have to answer any questions if you do not want to. You will not get any direct benefits if you choose to join the research study. You will not lose any services, benefits or rights you would normally have if you decide not to join. Taking part in the research study will not cost you anything. You will not be paid for being in this research study. Completing and submitting the online survey is taken to mean consent to participate.

There are no risks associated with participation in this study.

This research study will be written up as a research report. The report will be available on the university library website. If you would like to receive a summary of this report, I will be happy to send it to you.

If you have any questions during or afterwards about this research study, feel free to contact me or my supervisor on the details listed below. If you have any concerns or complaints about the ethical procedures of this research study, you are welcome to contact the University Human Research Ethics Committee (Non-Medical), telephone +27(0) 11 717 1408, email hrecnon-medical@wits.ac.za.

Yours sincerely,
Nkhumeleni Motsage

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Appendix B: Ethical Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Research Office

HUMAN RESEARCH ETHICS COMMITTEE (NON-MEDICAL)
R14/49 Motsage

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER: H23/09/26**
PROJECT TITLE	Knowledge, attitude and perception on Importance of Pharmacovigilance by Pharmacists in Pharmaceutical Companies in South Africa
INVESTIGATOR(S)	Mrs N Motsage
SCHOOL/DEPARTMENT	Pharmacy and Pharmacology/
DATE CONSIDERED	15 September 2023
DECISION OF THE COMMITTEE	Approved Risk Level: Minimal
EXPIRY DATE	22 February 2027

DATE 23 February 2024 **CHAIRPERSON** _____
(Professor J Watermeyer)

cc: Supervisor : Dr N Padayachee

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **A SIGNED COPY** returned to the Secretary electronically. Unreported changes to the application may invalidate the clearance given by the HREC (Non-Medical)

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure be contemplated from the research procedure as approved I/we undertake to submit an amendment of the protocol to the Committee. **I/we agree to completion of a regular progress report. For Minimal and Low Risk studies, this is due annually on 31 December. For Medium and High Risk studies, this is due twice annually on 30 June and 31 December.**

_____ 23-Feb-2024
Signature **Date**

PLEASE QUOTE THE PROTOCOL NUMBER ON ALL ENQUIRIES