
**College of Health Sciences**

**School of Pharmacy**

**Department of Pharmaceutics and Social Pharmacy**

# Pharmacovigilance System in Ethiopia: Implementation Status and Challenges

**By**

**Sisay Endale**

June, 2021

Addis Ababa, Ethiopia

Addis Ababa University

College of Health Sciences

School of Pharmacy

Department of Pharmaceutics and Social Pharmacy

# Pharmacovigilance System in Ethiopia: Implementation Status and Challenges

By

Sisay Endale

**Under the supervision of;**

Professor Teferi Gedif

Tesfa Maraew (M.Pharm)

A Thesis Submitted to the Department of Pharmaceutics and Social Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University for the Partial Fulfillment of the Requirements for the Degree of Master of Science in Regulatory Affairs (Medicine Regulation Track).

June 2021

Addis Ababa, Ethiopia

Addis Ababa University

School of Pharmacy

This is to certify that the thesis prepared by Sisay Endale Biru entitled: Pharmacovigilance System in Ethiopia: Implementation Status and Challenges and submitted in partial fulfillment of the requirements for the degree of Master of Science in Regulatory Affairs (Medicine Regulation Track) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by the Examining Committee

**Internal Examiner**: Dr. Eskinder Eshetu Signature: ----------Date: ----------

**External Examiner:** Dr. Solomon Mequanente Signature: ---------- Date: ----------

**Advisors:**

Professor Teferi Gedif Signature: ---------- Date: ----------

Mr. Tesfa Marew Signature: ---------- Date: ----------

_____

Head of Department

# Abstract

**Background**: Functional pharmacovigilance system is vital to ensure patient safety in the healthcare system. In the Ethiopian context, there is paucity of information on the organizational functionality of the pharmacovigilance program.

**Objectives:** To assess the Pharmacovigilance system and implementation status in Ethiopia

**Method**: An institution-based mixed study design was used to assess the pharmacovigilance functionality at hospitals, pharmaceutical companies, and regulatory authority. World health organization's pharmacovigilance indicators and key informant interviews were used for data collection. Quantitative and qualitative data were analyzed using Microsoft excel (2013) and thematic analysis approach, respectively.

**Results**: Only 1 (3.3%) of the 30 hospitals had pharmacovigilance unit with dedicated budget, 3 (10%) had staff assigned, and 7 (23.3%) had SOP. Similarly to hospitals, out of 32 pharmaceutical companies 4 (12.5%) had separate pharmacovigilance unit, 12 (37.5%) had regulatory unit, and 5 (15.6%) had budget for Pharmacovigilance. The national pharmacovigilance center have most of the structure, process, and outcome level pharmacovigilance practices. As significant challenges, resource constraints and reporting-related issues were identified. Patient harm, loss of confidence and trust, increased circulation of unsafe products, and economic costs reported as significant consequences. Sector experts recommended increasing training, engaging sector stakeholders, and improving the regulatory system as key interventional strategies.

**Conclusion**: There are substantial variations in the structures, processes, and outcomes of pharmacovigilance status among the studied organizations. Most pharmacovigilance system indicators are absent in the majority of pharmaceutical companies and hospitals. However, most of the elements of Pharmacovigilance systems are exercised by the national regulatory authority.



**Keywords**: Adverse drug events, Pharmacovigilance System, Pharmacovigilance Indicators

## Acknowledgments

Above all, I would like to thank the Almighty God with his mother Virgin St. Mary for giving me the will, courage, and strength to pursue and accomplish this study. I am very much grateful to my advisors Professor Teferi Gedif and Mr.Tesfa Marew for their continuous encouragement, scholastic exchanges on the topic, and spending their time reviewing the document, adding valuable comments and feedback for the compilation of this final thesis work.

My thanks go to the Department of Pharmaceutics and Social Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University for sponsoring my study and for the unreserved support and cooperation extended throughout the study. I am also indebted to my colleagues and friends for their moral support and encouragement throughout the study.

My special gratitude also goes to participants of the study including study organizations and key informants who willingly provided me the necessary data and information for the conduct of the study.

Finally, I would like to thank all my families and relatives as this thesis would not have been possible without their continuous encouragement and support.

## Table of Contents

# List of Figures

# List of Tables

# List of Abbreviations/Acronyms/

| | |
|---|---|
| ADEs | Adverse Drug Events |
| ADRs | Adverse Drug Reactions |
| AEs | Adverse Events |
| EFDA | Ethiopian Food and Drug Authority |
| EFMHACA | Ethiopian Food, Medicine and Healthcare Administration and Control Authority |
| HCPs | Healthcare Professionals |
| IPAT | Indicator-Based Pharmacovigilance Assessment Tool |
| KIs | Key Informants |
| LMICs | Low and Middle-Income Countries |
| MAHs | Marketing Authorization Holders |
| MEs | Medication Errors |
| MRIS | Medicine Registration Information System |
| NMRAs | National Medicines Regulatory Authorities |
| NPC | National Pharmacovigilance Center |
| NRA | National Regulatory Authority |
| PMS | Post Marketing Surveillance |
| PSURs | Periodic Safety Update Reports |

| | |
|---|---|
| PV | Pharmacovigilance |
| RA | Regulatory Authority |
| RMP | Risk Management Plan |
| SOPs | Standard Operating Procedures |
| SSA | Sub-Saharan African Countries |
| UMC | Uppsala Monitoring Centre |
| WHO | World Health Organization |

# 1. Introduction

## 1.1. Background

Maintaining and promoting patient safety is the main target behind a health care system. When it comes to a patient's safety, medicines are the most important factors which could cause adverse outcomes. To minimize this, pharmacovigilance (PV) is an essential tool in the clinical use of medicines for patients and protects public health. The World Health Organization (WHO) defined PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems" (WHO, 2002a, 2004). It plays a pivotal role in ensuring the ongoing safety of medicinal products following tragic incidences such as the thalidomide episode in the 1960s (Venulet and Helling-Borda, 2010; Kim and Scialli, 2011).

An efficient and properly working PV system is crucial to use medicines safely, effectively, and with confidence. A functional PV system enables to ensures the safety and effectiveness of medicines and protects the public through efficient and timely identification, collection, analysis, and management of medicine-related adverse events (AEs) and communicates the risks and benefits for decision (Eguale *et al.*,2008*).* A strong PV system requires coordinated, interdependent functioning of activities, mobilization of sector resources, and engagement of different stakeholders at all levels to improve overall medicine safety (WHO, 2015).

To protect the public from unsafe medicinal products, the PV system should be able to achieve optimal functioning capabilities. Implementation of a well-functioning PV system is a coordinated responsibility from different partners including pharmaceutical manufacturers, regulators, health institutions, academic and research institutions, healthcare workers, media, and consumers (Suleman, 2010). To achieve the goal, a country's PV system should incorporate activities and resources at the facility, national, and international levels and foster

collaboration among the partners and organizations that contribute to ensuring medicine safety (WHO, 2004).

Ethiopia has established its PV program under the then Ethiopian Food, Medicine, and Healthcare Administration and Control Authority (EFMHACA) currently called the Ethiopian Food and Drug Authority (EFDA). Ethiopia is an official member of the WHO International Drug Monitoring Center at Uppsala (UMC) (Isah *et al.*, 2012). EFDA proclamation no 1112/2019, Article 4 sub-article 9 mandated the authority to carry out post-marketing surveillance (PMS) activities to ensure the safety, efficacy, and quality of medicines and appropriate legal measures for patient safety and better treatment outcome for products marketed in the country (EFDA, 2019).

In 2002, the EFDA spontaneous Adverse Drug Reaction (ADR) reporting was initiated and healthcare professionals (HCPs) have been encouraged to report ADRs using the ADR reporting form and made available throughout all health facilities. The authority is mandated to investigate safety concerns and take appropriate actions to prevent and minimize medicine-related harm, and developed PV guideline (EFMHACA, 2014, Mulatu and Worku, 2014). To date, there is a lack of comprehensive and multi-stakeholder-based PV system assessment study on pharmaceutical companies, health facilities, and the regulatory authority (RA). This study was aimed to assess the PV system of selected pharmaceutical companies, health facilities, and the national regulatory authority (NRA) with particular emphasis to current implementation status, major challenges, and interventional strategies.

## 1.2. Statement of the Problem

The demand and access to new and essential medicines for the management of different health problems is increasing in both developed and developing countries. As a result, important lifesaving medicines are available to the public under different schemes but with both potential benefits and harms to the end-user (Isah *et al*., 2012). The possibility of harm is higher at times when adverse reactions could not be effectively detected and managed through appropriate PV systems (WHO, 2006).

Poor product quality, ADRs, medication abuse/misuse, and medication errors have a huge impact on the health care system and overall socio-economy of a nation (Lopez-Gonzalez *et al.*,2009; Mouton *et al.*, 2016). ADRs are among the leading causes of morbidity and mortality across the world. In Europe, it is estimated that 197,000 deaths per year are due to ADRs (Bouvy *et al.*, 2015; Santoro *et al.*, 2017) and claimed as the fifth most common cause of hospital deaths (Härmark and Van Grootheest, 2008). According to studies in Africa, ADR is an important cause of morbidity and the median prevalence of suspected ADRs on hospital admission was estimated as 8.4% *(*Mekonnen *et al.,* 2018). In addition, the circulation of counterfeit and substandard medicines has become a significant public health threat particularly seen in resource-limited countries eroding public confidence in the healthcare systems (Cockburn *et al.*, 2005; Caudron *et al.*, 2008).

Unlike the developed countries, most low and middle-income countries (LMICs) lack the system to ensure the safety of medicines. Their PV system is still in its infancy, underfunded, and not supported by effective legal or regulatory provisions. Nevertheless, a few of them could collect sufficient and important local safety information to perform independent risk/benefit assessments (Abiri, O.T & Johnson, W.C.N, 2019).). Studies suggest that about 96% of the developed nations have functional local PV systems, while only 27% of LMICs

have such systems (Hussain and Hassali, 2019). The law numbers in LMICs are usually attributed to the absence of requisite infrastructure and resources (Atia, 2019).

In most African countries, access to medicines is rapidly increasing but there is inadequate PV system and regulatory capacity to properly monitor and manage drug safety profiles (Olsson *et al.*, 2015). The increasing numbers of clinical studies, mass immunizations programs in most Sub-Saharan African (SSA) countries underscore the need for developing/strengthening the PV system. The region is characterized by a lack of quality medicines, shortage of competent local manufacturing firms, inefficient procurement and logistics management practices, significant prevalence of counterfeit/substandard medicines, ineffective regulatory and border control systems (Isah *et al.*, 2012). Though most African countries have become members of WHO's collaborating center for drug monitoring, very few have fully operating systems. Moreover, data on the burden of medicine-related harms in the continent are very scanty (Olsson *et al.*, 2015). Besides, the system remained understaffed, underfunded, and often without strong legal or regulatory provisions (Olsson *et a*l., 2015). There is an alarmingly high rate of under-reporting of ADRs by health professionals in most of the countries including Ethiopia (Ampadu HH *et al.*, 2016).

PV requires the involvement of different stakeholders including pharmaceutical companies, health institutions, and RAs. In this regard, the pharmaceutical industry poses a major challenge to the growth of PV as observed in most African countries (Pirmohamed *et al.*, 2007). Although marketing authorization holders (MAHs) have the responsibility to collect safety-related data and share with respective RAs with the stipulated timeline and the risk-benefit balance should be communicated, most of the companies didn't perform this activity (Mammì *et al.*, 2013). A study conducted in selected SSA countries showed that the involvement of the pharmaceutical industry in PV was found minimal. Among the studied pharmaceutical companies (n=21), only 8 of them had unit or staff responsible for PV activities, 5 of them had a standard operating

procedure (SOP) or reporting form for PV, and only 3 of them conducted phase 4 studies (Isah *et al*., 2012).

The involvement of HCPs in PV reporting is also negligible. A study conducted in Ethiopia highlighted that only a few reports are sent to the national PV center (NPC). Since its establishment, the number of ADR reports received from HCPs to the NPC is very small (Gurmesa and Dedefo, 2016). A study conducted in Gondar, Ethiopia from 2013 to 2015 showed that 815 chemotherapy-related ADRs were identified from 203 patients' medical files which were not reported (Belachew *et al.*, 2016). Similarly, six years of data (2002-2007) in Ethiopia showed that only 238 reports were sent to the NRA (Ermias *et al.*, 2011).

There is little data on the effectiveness and functionality of the PV system, and stakeholders' based investigation was not carried out to systematically assess the status of PV systems, progress made, and underlying factors in Ethiopia. Therefore, this study tried to assess the structure, process, and outcomes of PV status, practices, and activities in selected pharmaceutical companies, hospitals in Addis Ababa, and the NRA.

### 1.3. Significance of the study

A well-functioning PV system safeguards the public through efficient and timely identification, collection, assessment, and communication of medicine-related AEs (SPS, 2011). To achieve this goal, it is essential to have a functional PV system for each respective stakeholder. In this regard, proper investigation of PV system status, practices, and activities among those important stakeholders in the country is vital to align the country's PV system with global healthcare best practices.

Evaluating the current status, identifying weaknesses and potential barriers for implementation of the PV system in the country will enable to improvement of the existing PV system through designing effective strategies and take the necessary action for further improvement. The result

of this study will also provide baseline data for the NRA and other stakeholders such as health facilities, pharmaceutical companies, and others who have direct or indirect involvement in the provision of medicines safety and provides general recommendations that need to be discussed to help the stakeholders. Finally, the study may open the eyes of other researchers to conduct other studies in the area and the evidence from this study will contribute to the scientific community.

# 2. Literature Review

## 2.1. Adverse Drug Events

ADE is a general term that is described as any untoward medical occurrence that may be presented during treatment with medicine but does not necessarily have a causal relationship with the treatment (UMC, 2013). It indicates an injury caused by a drug-related medical intervention. In the regulatory setting, AEs are categorized as ADEs indicating harmful and unintended consequences of medication use, and a leading cause of unplanned hospital admissions and death. Their detection, documentation, and reporting are fundamental to PV activities (Budnitz, D. S., *et al*., 2011).

ADEs are common complications of clinical care resulting in significant morbidity, mortality, and high clinical expenditure comprising the largest single category of AEs encountered by hospitalized patients, accounting for a large proportion of all injuries. The occurrence of ADEs is associated with increased morbidity and mortality, prolonged hospitalizations, higher costs of care, additional resource utilization, time away from work, and lower patient satisfaction (UMC, 2013). It is estimated that 1 in 5 hospital injuries or deaths is secondary to an ADE, with an annual prevalence of up to 450,000 injuries in the US (Zhou L and Rupa A., 2017).

ADEs are a global concern for healthcare policy-makers, healthcare professionals, and the public (Aljadhey, H. *et al*., 2013) and place a huge burden on healthcare systems due to the resources needed to diagnose and treat the symptoms and diseases they cause. From the perspective of society, these costs are unnecessary, regardless of the point of origin. A micro-costing study in Germany used routine data to extrapolate the annual total costs, reporting a price tag of about 1 billion Euros (Rottenkolber, D., Hasford, J., & Stausberg, J., 2012). In addition to the economic consequences, cases of AEs affect the reputation (credibility) of the health system leading to loss of trust (Swain, S., & Patra, C., 2014).

Estimating the true incidence of ADE in the general population is difficult, with uncertainty about the number of patients exposed to a given drug, insufficient documentation and underreporting, as well as the effect of publicity around a particular drug on the reported frequency of an event. A recent international study using hospital datasets estimated the prevalence of ADEs to be 3.2% in England, 4.8% in Germany, and 5.6% in the USA (Stausberg, J., 2014).

ADEs includes ADRs, product quality defect (PQD), and medication errors (MEs). ADEs from PQD, ADRs, and MEs significantly contribute to morbidity and mortality. ADRs is defined by WHO as "any noxious, unintended, and undesired effect of a drug that occurs as a result of treatment with a drug at normal doses used in man for diagnosis, prophylaxis, and treatment" (WHO, 2004). It has become a concern for public health systems around the world, adding to the burden of total treatment costs for patients (Palappallil, D. S., 2017).

ADRs are of great concern to policymakers as they are a major cause of morbidity and mortality in hospitals (Mahmoud M. A, 2014 *et al.,* McKay, A. J. *et al*., 2015) resulting in a considerable economic burden both to patients and society as a whole (Gyllensten, 2013). In many countries, ADRs rank among the top leading causes of mortality and morbidity (Najafi, S., 2018). It remains a challenge in modern healthcare, particularly with the increasing complexity of therapeutics, an aging population, and rising multi-morbidity (Coleman, J. J., & Pontefract, S. K., 2016). It varies in magnitude; in its severe form may cause morbidity, mortality, hospital admissions, risk of readmission, increases the length of hospital stay, and other negative effects (Angamo, M. T, 2016; Walter, S. R, 2017). In addition, ADR affects the quality of life of patients and the hospital system (Rolfes, L, 2016).

On the other hand, MEs are described as "any preventable event that could cause or lead to inappropriate medication use or patient harm while the medication is in the control of the HCP patient, or consumer. Such events may be related to professional practice, health care products,

procedures, and systems, including prescribing, order communication, product labeling, packaging, nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use" (NCCMERP, 2015). They are mishaps that occur during prescribing, transcribing, dispensing, administering, adherence, or monitoring a drug.

About 25% of ADEs are caused by MEs which can occur at any stage of the medication-use system, including preparation, prescription transcription, dispensation, storage, administration of drugs, and patient and compliance; however, the most common errors take place during prescribing and administration (Pote, S., Tiwari, P., & D'cruz, S., 2007). Of these 28% were identified as preventable (Eyal Zimlichman, M. D. *et al*., 2018). The latter is further accompanied by additional costs of more than US$3000 per patient with an extended hospitalization of 3 days (Hug B. L. *et al.*, 2012). According to the American Society of Health-System Pharmacist (ASHP) in 2014, MEs can include prescribing errors, omission errors, wrong time errors, and unauthorized drug errors, wrong dosage form errors, improper dose error, wrong drug preparation errors, wrong administration or technique errors, monitoring errors, deteriorated drug errors, and compliance errors" (Alshakka, 2017).

## 2.2. The Scope of Pharmacovigilance

PV was primarily related to ADRs that are adverse effects where there is a confirmed or suspected causal relationship. At present, the scope of PV has expanded to include other medication safety issues such as medication errors, counterfeit or substandard medicines, lack of efficacy of medicines, misuse and/or abuse of medicines, and interaction between medicines. The concern of PV is not limited to modern medicines but also includes complementary and alternative medicines. It also includes regulating the safety of blood products, vaccines, and medical devices (WHO, 2015).

## 2.3. Stakeholders in Pharmacovigilance

Globally, the utilization of drugs is increasing due to various reasons calling for important measures to assure the safety and effectiveness, and management of the risks associated with their use. Effective implementation of the PV system requires close and effective collaboration among the different stakeholders including pharmaceutical companies (manufacturers, importers, wholesalers, distributors, and retailers), RAs, HCPs, patients or patient parties, research organizations, health facilities, media, and WHO (Davies,2006). The stakeholders can contribute to the establishment of functioning PV systems where the ultimate success depends on the commitment and from the government and a collaborative approach (Suleman, 2010; Palaian, 2018).

As key stakeholders, pharmaceutical manufacturers and distribution outlets do have the responsibility for the safety of medicines. Pharmaceutical manufacturers are particularly are expected to monitor the safety of medicines throughout the entire life cycle of the products (Talbot and Nilsson, 1998). Regulators on the other hand should continuously assess the information gathered from the spontaneous reports from health professionals, patients, and pharmaceutical companies. They also play an essential role to ensure the pharmaceutical companies are complying with regulations and duly fulfilling their PV obligations by conducting PV-specific inspections and if necessary take appropriate actions.

The effectiveness of the national PV system is directly dependent on the active participation of HCPs. They are in the best position to report any suspected ADRs observed in patients during their daily practice. For their vital role in the PV system, HCPs are expected to have enough knowledge, training, and skill in the field of PV for early recognition, management, and reporting of medicines safety issues (WHO, 2002b). Furthermore, they should be well educated about the necessity and procedure of AEs reporting and possess a combination of training and research skills in the area. Despite global concerns against medication safety, there is a lack of

awareness and knowledge of PV and ADR reporting among HCPs. Moreover, in developing countries, recent studies indicated that ADRs are poorly reported by HCPs where only 2-4% of all adverse reactions and 10% of serious ADRs are reported worldwide. This indicates that medicine safety assessment must be considered an inseparable part of everyday clinical practice for HCPs (Almandil, 2016). The main stakeholders and their relationship in PV are indicated in Figure 3 below (WHO, 2015).

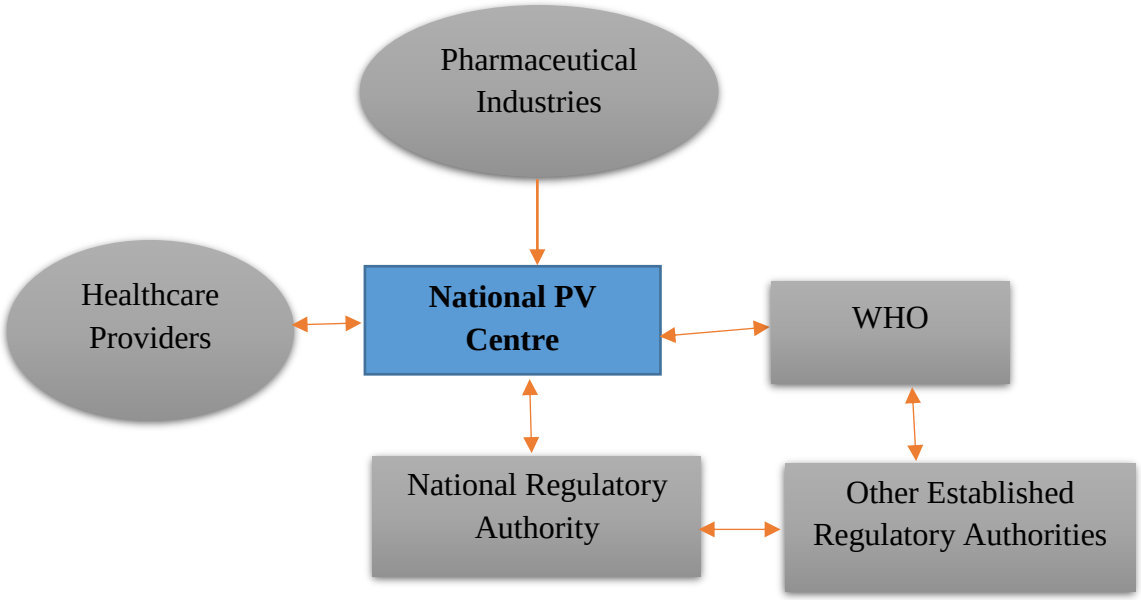


**Figure 1:** Diagrammatic representation of various stakeholders in the PV system (WHO, 2015)

## 2.4. Functions of Pharmacovigilance Systems

PV is an essential component of public health safety which enables quantifying previously recognized ADRs, identify unrecognized ADEs, evaluate the effectiveness of medicines in real-world situations, and decrease mortality and morbidity associated with ADEs (Eguale *et al*., 2008). A comprehensive PV system is much more beyond risk identification and data collection; it also undertakes risk evaluation, minimization, and communication. Such systems to protect the public through efficient and timely detection, assessment, reporting, and

communication, of medicine-related AEs through people and structures enables RAs to take appropriate action (SPS, 2009).

The consultation forum held by the WHO in 2010 and subsequent review by the WHO advisory committee on the safety of medicinal products identified some of the expanded roles of PV for a national health system. These include: identifying signals of drug safety; undertaking risk assessment and risk management; providing effective communication on drug safety issues to prevent and promote public health; supporting individual patients and national health systems through effective policies and guidelines; and maintaining up-to-date drug utilization information (WHO, 2002a).

## 2.5. Features of Pharmacovigilance System in Resource-Constrained Settings

In most developed countries, monitoring the safety of drugs aftermarket authorization is mandated to different stakeholders. MAHs are legally required to collect, investigate, and submit ADEs and Periodic Update Reports (PSURs) concerning the product, even if these events occur in other markets. Similarly, HCPs are professionally obliged to report ADEs and medicines safety-related issues to relevant RAs. Regulators on the other hand are expected to develop and implement a variety of tools to manage the safety of products authorized to be marketed. Developing countries rely on the comprehensive PMS that exists in developed countries to identify the risks and benefits of drug products (Olsson *et al.*, 2010).

An effective PV system is more essential for resource-limited settings for a variety of reasons including to significantly increase availability and use of relatively new essential medicines, weak or nonexistent system for PV implementation, lack of systematic approach to address medicines safety issues, and varying susceptibility profile of patients for ADEs due to genetic, nutritional and other differences (Nwokike, 2008). A WHO estimation report indicated that at least 30% of national medicines regulatory authorities (NMRAs) in developing countries have limited capacity to perform the core regulatory functions. For example, most of NMRAs in

Africa were unable to perform major functions expected from a standard NMRA. Another WHO report indicated that only 7% of African countries could develop a modest capacity while more than 90% of them have either minimal or no capacity to execute core regulatory functions (WHO, 2016).

A national PV system assessment from various African countries revealed that the PV system was found at the infancy stage. A medicine safety system assessment conducted in Rwanda using an indicator-based PV assessment tool (IPAT) indicated that the majority of the structural, process, and outcome indicators of functional PV systems were missing. PV policy had not been approved and relevant laws requiring regulation of medicines were missing. Furthermore, the PV center and its guidelines were not approved; pre-service and in-service training on PV were lacking; formal mechanisms of medicine safety information were absent; and PV activities to monitor patient safety were found to be uncoordinated and fragmented (Nwokike and Joshi, 2009).

A similar study in Ghana identified that basic structures existed for improving PV system. However, processes and outcomes indicators that mark well-functioning PV systems were found to be deficient (Nwokike and Eghan, 2010). Another comparative study conducted in SSA countries using IPAT showed that some form of PV activities were practiced in most of the countries but there was a lack of coordination among all the components of the PV system affecting the capacity to ensure quality, efficacy, and safety of medicines (Kuemmerle *et al*., 2011).

Assessment of PV activities in LMICs highlighted deficiencies regarding the structural, process, and outcome indicators calling for an urgent need for identification and implementation of feasible systems, governance mechanisms, infrastructures, human resource and application of innovative strategies in PV (Olsson *et al*., 2010; Allabi and Nwokike, 2014).Various other studies have also indicated poor knowledge and attitude of HCPs towards

PV adversely affecting the capacity of the system to monitor the safety of medicines ( Doua and Geertruyden, 2014; Caturla Goñi, 2016).

### 2.6. Emerging Challenges of Pharmacovigilance

The main reason behind the establishment of PV system is to improve scientific understanding of the safety profile of drugs and advise RAs for evidence-based decision making (Lindquist and Edwards, 2001). These days, PV has emerged over time as an essential part of public health but facing different challenges to develop better health care systems. Some of the identified challenges include globalization and increased web-based product sales and information flow, the requirements for broader safety concerns, the disparity between public health and pharmaceutical industry interests among developing countries, emerging economies, and developed countries, and the difference in attitude and perceptions regarding the benefits, harm, outcomes and overall impact (Biswas and Biswas, 2007).

Globalization becomes a key challenge as it facilitates free trade and communication across borders and increasing use of the internet has resulted in the rapid dissemination of drug information and access to medicinal products. Globalization-driven changes resulted in new kinds of safety concerns including illegal purchasing of medicines through the internet, increased habit of self-medication, public exposure to substandard and unfit products, etc. (Almenoff, 2007). The rapid and widespread growth of electronic communication technology commonly presents some challenges in the context of drug safety monitoring and reporting (CIOMS, 2001; WHO, 2001). On the other hand, web-based sales and promotional activities contribute their part to the challenge in PV such as drug advertisements with unreliable claims ranging from prescription medicines, unregistered drugs, and controlled substances to herbal medicines with suspicious quality and safety. Aggressive promotion by drug companies often results in the unnecessary and irrational use of medicines by consumers (Härmark and van Grootheest, 2012).

Drug utilization patterns also pose a challenge to the PV system. Irrational drug use, frequent self-medication practice, and lack of regulatory control mechanisms over drug sales aggravate the risk of adverse effects. The presence of high illiteracy, additional use of traditional medicines, and the increasing trend of substandard medicines in developing countries further complicate the existing risk. PV programs should, therefore include public awareness and education about the rational use of medicine to ensure better healthcare in all countries. It is also required to provide the required drug safety information and the information needs to be accessible to the general public to guarantee the vital role of patients in the rational safe use of medicine (Kumar, 2013).

Overall, all PV systems are facing common challenges in drug safety surveillance. To control the existing challenges, requires working in five principal interrelated areas such as increasing the engagement of the public, strengthening cooperation and partnerships, incorporating modern information-sharing systems, adopting a global approach, and assessing the impact of effort (Dal Pan, 2014).

## 2.7 Structural, Process and Outcome Indicators Used to Measure and Assess Pharmacovigilance Performance

The development of performance metrics for PV systems requires common agreement on what the scope of such a system includes. Performance metrics are required to enable standardized, consistent, and routine monitoring and evaluation of PV, and such a tool are useful in establishing the current capacity for safety monitoring and will allow measurement of progress. In the health sector, performance metrics or indicators have been defined as measures of structure, process, and outcomes of health care that can be used to guide and monitor the quality and appropriateness of health care delivery with the aim of health care improvement (SPS, 2009).

In 2015, WHO developed a set of PV indicators to measure the status and development of PV systems in health facilities and countries. These indicators are important to identify gaps and the need for further investments (WHO, 2015). The structural, process, and outcome indicators will reflect the existence of PV facilities, the dynamics in the set-up, and the eventual outcomes, respectively.

The structural indicators assess the existence of key PV structures, systems, and mechanisms in the setting being studied. The availability of basic infrastructure is required to enable PV operations. These indicators assess the elements that give visibility to PV. They also assess the existence of a policy and regulatory framework which enables PV to operate. By their nature, these indicators are essentially qualitative (WHO, 2015).

The process indicators measure (assess) the extent (magnitude) of PV activities. They focus on the constellation of activities that describe the mechanism of PV such as collection, collation, analysis, and evaluation of ADR reports. The indicators under this category measure directly or indirectly the extent to which the system is operating. The outcome indicators measure the final effects (results and changes) obtained through PV activities. They measure the extent of realization of the PV objectives which, in essence, constitute ensuring patient safety (WHO.2015).

## 2.8. Conceptual framework of the study

After an in-depth review of previous studies in the area and understanding the thematic elements, the following conceptual framework was adapted and contextualized for this particular study. The framework below (Figure 2) depicts the various factors which may have a direct and indirect impact on the overall functioning and implementation of PV system in the country. PV system implementation is influenced by the presence and absence of structure and process indicator resources (financial, human, legal, technical, and social), reporting mechanism, regulator system and capacity of the country, and data management techniques.

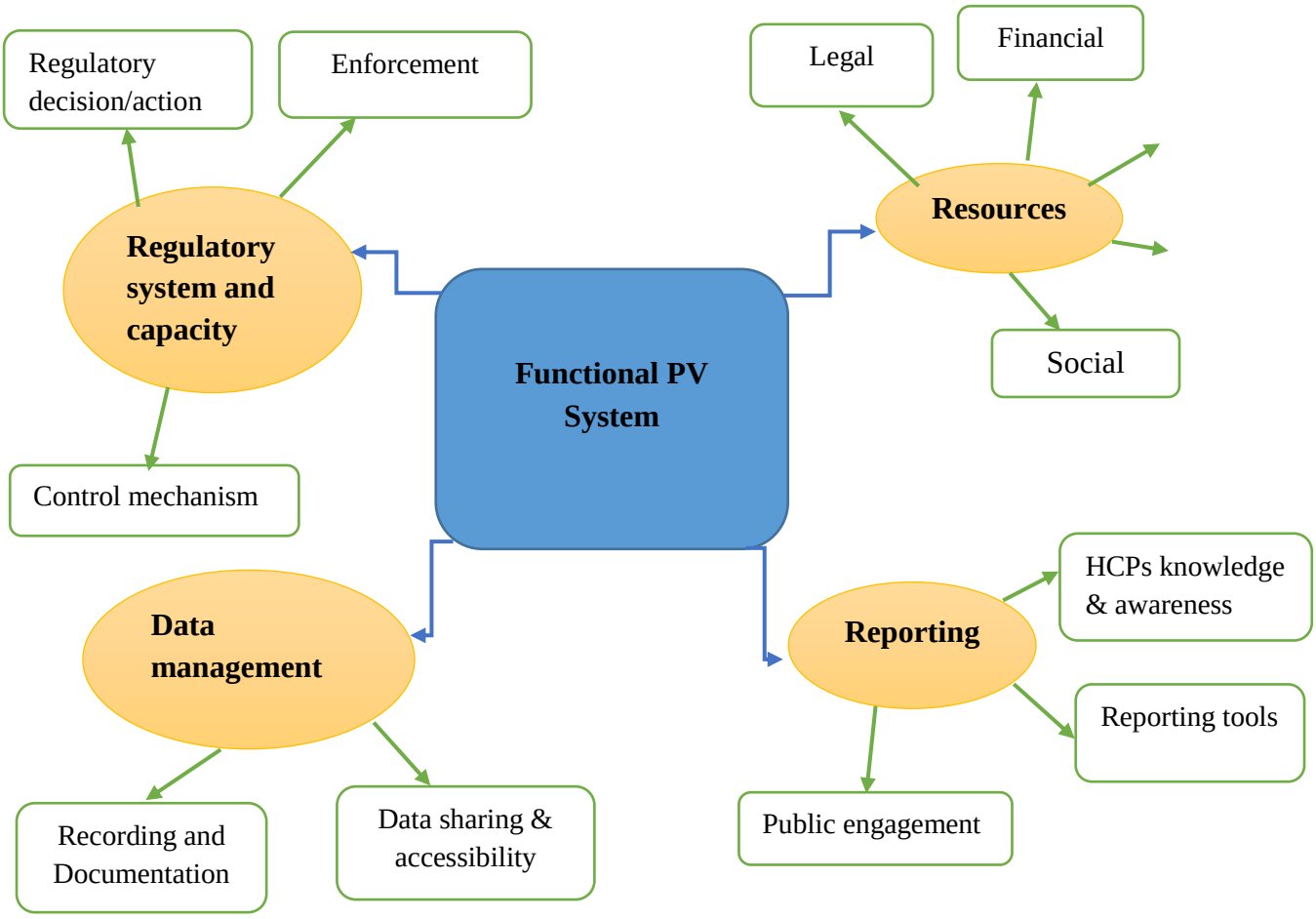


**Figure 2:** Conceptual framework used in the qualitative data analysis (Adapted from Elshafie *et al*., 2018b)

# 3. Objectives of the Study

## 3.1. General Objective

- To assess the PV system and its implementation status in Ethiopia.

## 3.2. Specific Objectives

- To assess structure, process, and outcomes of the PV system in Ethiopia.
- To assess the perception and contribution of HCPs in PV system implementation.
- To identify key challenges and opportunities for implementation of the PV system in the country.

# 4. Methods

## 4.1. Study Area and Period

The study was conducted in selected pharmaceutical companies, hospitals from Addis Ababa, and the NRA. In Ethiopia, there are 11 licensed and actively operating local medicine manufacturers, over 383 importers, and 6 multinational manufacturers having offices and undertaking their sales and marketing operations. Also, there are 36 (13 government, (1 defense, 1 police, 6 municipal, and 5 federal) and 23 private) hospitals in Addis Ababa of which 3 are specialized, 30 are general hospitals and the remaining 3 are primary hospitals. The specialized and general hospitals were chosen considering that they are the highest level of care facilities managing various levels of disease and use a range of classes of medicines, high incidence of medicine-related admissions and thus are likely to encounter medicines safety problems. The study was conducted from August 2019 to April 2020.

## 4.2. Study Design

An institution-based mixed concurrent triangulation design involving both quantitative and qualitative data collection techniques was employed. This design involves a single study containing qualitative and quantitative data collection. Data collection and analysis were conducted at the same time frame. The qualitative study followed athematic analysis.

## 4.3. Source and Study Population

For institutions, all available hospitals (public and private) in Addis Ababa, pharmaceutical companies (local medicine manufacturers, importers, and multinationals) in the country, and the NRA were used as a source population and the study population was general and specialty hospitals in Addis Ababa, importers registered as primary local agents, local manufacturers which are not newly established and multinationals having marketing and sales coordinating offices in Ethiopia. For individual participants, the source population was all professionals

working at the respective institution and the study population was those purposively selected individuals having experience, role, responsibility, understanding of PV, and position in their respective institution. Key informants (KIs) were selected from the EFDA, government, and private hospitals in Addis Ababa and pharmaceutical companies including local medicine manufacturers, multinational manufacturers, and local pharmaceutical importers registered as primary agents.

### 4.4. Sample Size Determination, Sampling Technique, and Procedure

For the quantitative study, all general and specialized government and private hospitals in Addis Ababa were approached to participate in the study. From the total of 33 general and specialized hospitals, 30 hospitals (12 government and 18 private) were willing to participate in the study. The three hospitals (one government and two private) were not willing for an undisclosed reason. To determine the final sample size of local pharmaceutical importers, 25% of the total importers registered as a primary agent and accessible in the NRA's medicine registration information system (MRIS) database were used to calculate the final sample size. Accordingly, a total of 83 importers with registered products as primary agents were retrieved from the MRIS database. Of these, 21 (25%) importers were included. On the other hand, among the total 11 local medicine manufacturing companies, two new manufacturing plants were intentionally excluded from the study, and all the remaining (n= 9) local medicine manufacturers were approached and six of them participated in the study. Two local manufacturing companies were not willing to participate and one was under the process of closing the plant. In addition, five of the six multinationals were included (one company was excluded as it was unable to get the focal person in charge responsible for the provision of data during data collection). For the qualitative study, KIs were purposively selected from the NRA, pharmaceutical companies, and hospitals, and the final sample size was based on saturation (the point at which the data collection process no longer offers any new or relevant data).

Accordingly, saturation was reached after 18 KIs interviews, and three additional 3 KIs were included to check whether additional new ideas emerge or not making a total of 22 KIs.

## 4.5. Data Collection and Management

### 4.5.1. Data collection procedure

Before commencing the study, an explanatory statement detailing the objective of the study was given to the respective study organizations and individual KIs, and heads of the study institutions were contacted for their approval and access to data. The focal person in charge of PV provided interviewed and answer the study questions. The checklist was filled by data collector by interviewing the focal person. During filling of the checklist for a quantitative study, the interviewer cross-checked the presence of evidence for the objective assessment by asking the focal person to show evidence for the claim. For the qualitative study, an in-depth KI interview was conducted at their workplace. An interview took an average of 25 to 40 minutes and an audio record was used for those who are willing and a note was taken for those who refused to record their voice. Interviews were conducted by two pharmacists (the researcher himself and another colleague having prior experience in KI interview). Before conducting an interview, interviewers took online training courses on qualitative data collection procedure (technique), instrument, and analysis. Also, KIs were invited to describe their opinions in the national local language (Amharic) to give them freedom, and any ambiguity from the interviewee was cleared at the time of the interview.

### 4.5.2. Data collection instruments

For the quantitative part, a checklist adapted from the WHO PV assessment tool (2015) and contextualized to local situations to collect data to measure the presence or absence of structure, process, and outcome level PV activities and practices in this regard, from pharmaceutical companies, hospitals, and the NRA. For this purpose, both core and complementary PV indicators were selected and used for objective measurement for the presence or absence of

key infrastructures, activities, and outcomes. For the qualitative part, a semi-structured and investigator-administered interview guide with probing questions was developed for an in-depth interview.

### 4.5.3. Data quality assurance process

Before data analysis for the quantitative study, all checklists were cross-checked for their completeness. Some PV indicators which are not relevant or applicable to the study organizations are either removed or tailored to the study setting. For the qualitative part, three pilot interviews were conducted to check the relevance of the interview guide questions in terms of addressing study objectives and research questions and led to minor amendments of the interview guide such as the inclusion of additional probing questions, and removing of vague and leading questions.

The transcripts of the interviews were generated from audiotapes and notes taken and transcribed verbatim in Amharic, translated to English, and analyzed for issues and themes emerging from the text which was independently coded and verified by two independent individuals (principal investigator and another individual who has previous experience in qualitative research). The interview result was back-translated to compare translations with the original text for quality and accuracy and to evaluate the equivalence of meaning between the source and target texts. Also, interview data were analyzed as they were collected through the process of color-coding. Discrepancies during transcription, translation, back translation, and coding by the two individuals were reached into consensus through discussion with advisors.

## 4.6. Data Analysis and Interpretation

Quantitative data were analyzed using Microsoft Excel (2013) and the result of the categorical variables was mainly expressed descriptively using frequency and percentage. On the other hand, qualitative data were analyzed manually using themes with verbatim quotes from the participants. The qualitative thematic analysis mainly followed a deductive approach. Analysis

was started with predetermined codes to the data set and then find excerpts that fit those codes from the row data set (text from the interviews). The codes used in this approach were created from concepts drawn from the literature. Those issues not captured in the deductive analysis or those not fit with themes used in the deductive approach were coded inductively in which themes were generated by looking at patterns from the data set. In this approach, the researcher read through the data (texts from interviews) and allows codes to emerge. The codes were revised iteratively, and similar codes were grouped into themes. As the process continued, new themes emerged, and groups of related themes (sub-themes) were placed together under larger ones.

## 4.7. Ethical Consideration

Ethical clearance was obtained from the ethics review committee of the School of Pharmacy, Addis Ababa University (ERB/SOP/67/04/2019), and official letters of support were written from the Department of Pharmaceutics and Social Pharmacy to the respective organizations. Before data collection, permission was obtained from all hospitals, pharmaceutical companies, and the NRA based on the letter of support and ethical clearance. Data were collected after a clear oral presentation of the aims and importance of the study. Oral informed consent was obtained from the organizations and KIs after a clear presentation of the purpose of the study and its benefit. Participants were assured about the confidentiality of their information obtained in the study by excluding any personal identifier in the data collection form and anonymization of quotes to prevent statements that could be traced back to individuals. Interviewees were assured and encouraged to talk about their views on this issue rather than about their company's position. Finally, KIs were asked their permission to record the interview and were informed and assured of the right to refuse or terminate at any point in the interview and the audio record from the interview only remained in the hands of the investigator.

## 4.8. Definitions of Indicators (WHO, 2015)

**Structural PV indicators**: are indicators intended to assess the existence of key PV structures, systems, and mechanisms in the setting being studied

**Process PV indicators:** are indicators that assess the extent of PV activities that focus on the constellation of activities that describe the mechanism of PV such as the collection, collation, analysis, and evaluation of ADR reports

**Outcome and Impact PV indicators**: are indicators that measure the final effects (results and changes) of PV activities. They measure the extent of realization of the PV objectives which in essence, constitute ensuring patient safety

**Core PV indicators**: are indicators considered to be highly relevant, important, and useful in characterizing PV

**Complementary PV indicators**: are indicators those additional measurements considered to be relevant and useful. They serve to further characterize the PV situation in the stated setting but need not be used in all instances

## 4.9. Researcher's Position and Reflectivity

Reflexivity is considered as an integral aspect of qualitative research which involves researchers understanding how processes of doing research shape its outcomes. Stating the researcher's position and reflexivity is important in understanding the epistemological and personal conviction of the individual researcher, which pertains to the analytic attention to the researcher's role in the research (Hsiung, 2008; Lambert *et. al*., (2010).

The researcher being a healthcare provider (pharmacist) working in the academic institution has been seen both as an opportunity and limitation in the research. Currently, the researcher is a pharmacist by profession working in an academic institution and doing his Master's degree in Regulatory Affairs (Medicine regulation track). The researcher didn't work at RA,

pharmaceutical companies, and health facilities including hospitals. As a result, KIs from the study organizations were free to give their view freely.

In the designing stage of the research, the researcher's inadequate training in qualitative research methods was difficult. The researcher only took a course entitled research method which covered an introductory aspect on qualitative research design and methods as part of fulfilling the Master's program. To minimize its impact on the overall research design, the researcher had extensively explored online qualitative study design training including analysis and presentation which enabled familiarize himself with the concept of qualitative research. In addition, interview guide question development, translation, back translation, coding, and theme development were done under the supervision of advisors. In the process of data collection, the researcher assessed interview guides used and amends some of the irrelevant and vague questions which enable to revise and modify the interview guide.

At the time of the study, the researcher was a novice researcher conducting qualitative research by interview method that required intensive and extensive interaction with participants. The researcher is a male and Amharic speaker, which also had an impact on data collection, created a common ground for some to discuss freely in interviews. Furthermore, the direct, face-to-face interaction that an interviewer has with an interviewee allows the researcher to gain a deeper understanding of the participants compared to other methods, by providing an opportunity for clarification, probing, and prompting.

# 5. Results

## 5.1. Quantitative Study

### 5.1.1. Background information on study organizations

In the study, a total of 30 general and specialty hospitals (12 government and 18 private) were included; of which 6 were teaching hospitals. Besides, 32 pharmaceutical companies (6 local medicine manufacturers, 21 local importers, and 5 multinational manufacturers and NRA were included. Summaries of the characteristics of study facilities are presented in Table 1 and Figure 4.

**Table 1:** Characteristics of hospitals included in the study, Addis Ababa, Ethiopia, 2020, (N=30)

| Characteristics | Ownership N (%) | | |
|---|---|---|---|
| | Government (N=12) | Private (N=18) | Total (N=30) |
| **Service level** | | | |
| General | 9 (75) | 18 (100) | 27 (90) |
| Specialty | 3 (25) | 0 (0) | 3 (10) |
| **Teaching status** | | | |
| Teaching | 4 (33.3) | 2 (11) | 6 (20) |
| Non-teaching | 8 (66.7) | 16 (89) | 24 (80) |

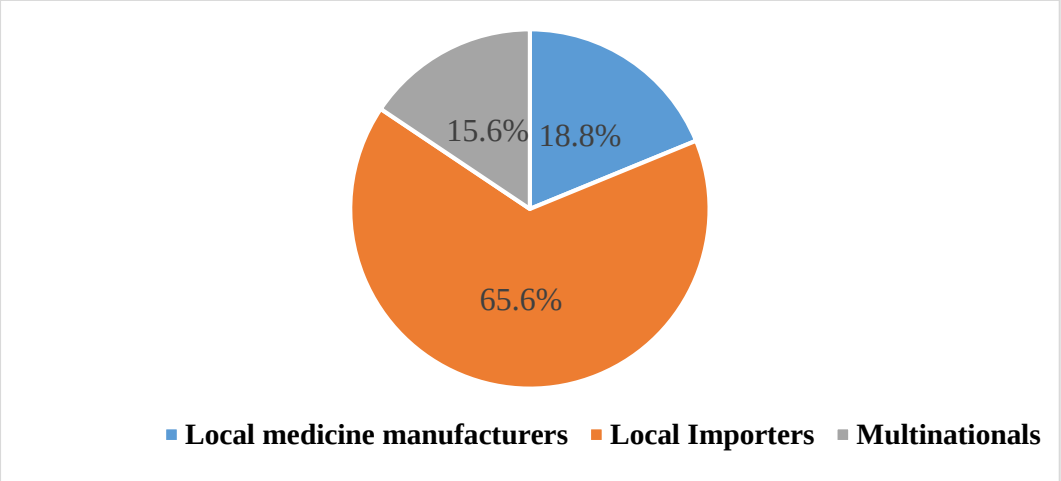


**Figure 3:** Pharmaceutical companies included in the study, Addis Ababa, Ethiopia, 2020, (n=32)

### 5.1.2. Structure, process and outcome of Pharmacovigilance practices and activities in hospitals

As observed in Table 2 below, almost all the hospitals in the study didn't have established PV units except one government hospital and other structural indicators are not sufficiently organized. The structure, process, and outcome levels of core and complementary PV indicators of the hospitals are summarized in the following tables (Table 2 and 3).

Regarding process PV indicators, most of the hospitals lack accurate documented (recorded) data. Due to the poor record-keeping practices of the hospitals, it was difficult to obtain and trace specific process PV performance indicators. As a result, the number (percentage) of hospitals that proclaimed 'Yes' (practice/exercise process PV indicators) but couldn't back it up with documented evidence (recorded data) and those which proclaimed 'No' (not practice/exercise process PV indicators) are narrated.

**Table 2**: Analysis of core structural Pharmacovigilance indicators in hospitals, Addis, Ababa, Ethiopia, 2020 (N=30)

| S/N | Core Structural Indicators | Response (N (%) | | | | | |
|---|---|---|---|---|---|---|---|
| | | *Government (N=12)* | | *Private (N=18)* | | *Total (N=30)* | |
| | | Yes | No | Yes | No | Yes | No |
| 1 | Presence of PV unit/department/ | 1 (8.3) | 11 (91.7) | 0 (0) | 18 (100) | 1 (3.3) | 29 (96.7) |
| 2 | Availability of human resources to carry out functions | 3 (25) | 9 (75) | 0 (0) | 18 (75) | 3 (10) | 29 (90) |
| 3 | Availability of regular financial provision for PV unit | 1 (8.3) | 11 (91.7) | 0 (0) | 18 (100) | 1 (3.3) | 29 (96.7) |
| 4 | Presence of written SOP for PV | 4 (3.3) | 8 (66.7) | 3 (16.7) | 15 (83.3) | 7 (23.3) | 23 (76.7) |
| 5 | SOPs signed, documented and officially adopted | 3 (25) | 9 (25) | 3 (16.7) | 15 (83.3) | 6 (20) | 24 (8) |
| 6 | Presence of medicine safety information dissemination tool | 4 (3.3) | 8 (66.7) | 0 (0) | 18 (100) | 4 (13.3) | 26 (86.7) |
| 7 | Availability of ADR reporting form in the setting | 11 (91.7) | 1 (8.3) | 16 (88.9) | 2 (11.1) | 27 (90) | 3 (10) |
| 8 | Process in place for collection and recording of ADR | 11 (91.7) | 1 (8.3) | 10 (55.6) | 8 (44.4 | 21 (70) | 9 (30) |
| 9 | Existence of newsletter/bulletin as a tool for PV information dissemination | 5 (41.7) | 7 (58.3) | 0 (0) | 18 (100) | 5 (16.7) | 25 (83.3) |

**Table 3:** Analysis of complementary structural Pharmacovigilance indicators in hospitals, Addis, Ababa, Ethiopia, 2020, (N=30)

| S/N | Complementary Structural Indicators | Response (N (%)) | | | | | |
|---|---|---|---|---|---|---|---|
| | | *Government (N=12)* | | *Private (N=18)* | | *Total (N=30)* | |
| | | **Yes** | **No** | **Yes** | **No** | **Yes** | **No** |
| 1 | Presence of dedicated computers for PV activities | 1 (8.3) | 11 (91.7) | 0 (0) | 18 (100) | 1 (3.3) | 29 (96.7) |
| 2 | Existence of computerized case-report management system | 0 (0) | 12 (100) | 0 (100) | 18 (100) | 0 (0) | 30 (100) |
| 3 | Existence of facility specific essential medicines list which is in use | 12 (100) | 0 (0) | 18 (100) | 0 (18) | 30 (100) | 0 (0) |
| 4 | Presence of functioning & accessible communication facilities for PV | 4 (33.3) | 8 (66.7) | 6 (33.3) | 12 (66.7) | 10 (33.3) | 20 (66.7) |
| 5 | Organization of PV training for health professionals | 2 (16.7) | 10 (83.3) | 1 (5.5) | 17 (94.5) | 3 (10) | 27 (90) |
| 6 | Availability of web-based PV training tools for health professionals | 0 (0) | 12 (100) | 0 (0) | 18 (0) | 0 (0) | 30 (100) |
| 7 | Presence of source of data on consumption and prescription of medicines | 7 (58.3) | 5 (41.7) | 10 (55.6) | 8 (44.4) | 19 (63.3) | 11 (36.7) |
| 8 | Presence of SOP for RMP | 0 (0) | 12 (100) | 1 (5.6) | 94.4) | 1 (3.3) | 29 (96.7) |
| 9 | Presence of reports that have processed & sent to RA | 10 (83.3) | 2 (16.7) | 6 (33.3) | 12 (66.7) | 1(53.3) | 14 (46.7) |

Due to the prevalence of inadequate documenting and reporting procedures in health facilities (hospitals), important process indicators that reflect on the constellation of activities that constitute the system of PV, such as the compilation (collection), collation, analysis, and assessment of ADR reports are lacking. Almost all health facilities (hospitals) surveyed do not keep copies of submitted forms, making it difficult to track adverse event reports. For example, 17 (56.7%) of the 30 surveyed hospitals (10 government and 7 private) said they reported ADR in the previous calendar year but didn't know how many ADR reports were filed, and 9 (30%) of the hospitals (7 government and 2 private) said they had total reports in the hospital database but couldn't provide recorded proof (documented evidence). Furthermore, 8 (26.7%) hospitals (5 government and 3 private) reported that total annual reports had been satisfactorily completed and submitted to the local PV canter in the previous calendar year but were not backed up by documentation. Except for one hospital, none of the others have had active surveillance activities in the last five years, either ongoing or completed.

Outcome indicators that measure the extent to which PV operations and goals are realized (results and changes) are rarely used or implemented. According to the findings, none of the hospitals investigated to use the core and complementary outcome indicators mentioned in annex (Annex III).

### 5.1.3. Structure, process and outcome Pharmacovigilance practices and activities in Pharmaceutical Companies

Table 4 and Table 5 below demonstrate the findings of both core and complementary structure, process, and outcome PV indicators collected from pharmaceutical firms including local producers, importers, and multinational manufacturers. As it is observed from Table 4, most of the structural elements of PV such as the presence PV unit, budget, personnel, etc. are not in place in the studied pharmaceutical companies.

**Table 4:** Analysis of core structural Pharmacovigilance indicators in selected pharmaceutical companies, Addis Ababa, 2020, Ethiopia (n=32)

| S/N | Core structural Indicators | Response (N (%)) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *Local Manufacturer* | | *Importer* | | *Multinational Manufacturer* | | *Total* | |
| | | Yes | No | Yes | No | Yes | No | Yes | No |
| 1 | Presence of regulatory unit in the company | 3 (50) | 3 (50) | 6 (28.6) | 15 (71.4) | 3 (60) | 2 (40) | 12 (37.5) | 20 (62.5) |
| 2 | Presence of PV unit/department/ in the company | 0 (0) | 6 (100) | 1 (4.8) | 20 (95.2) | 3 (60) | 2 (40) | 4 (12.5) | 28 (87.5) |
| 3 | Presence of human resources for PV unit | 0 (0) | 6 (100) | 2 (9.5) | 20 (90.5) | 2 (40) | 3 (60) | 4 (12.5) | 28 (87.5) |
| 4 | Presence of regular financial provision for PV | 1 (16.7) | 5 (83.3) | 0 (0) | 21 (100) | 4 (80) | 1 (20) | 5 (15.6) | 27 (84.4) |
| 5 | Presence of written SOP for PV | 3 (50) | 3 (50) | 3 (14.3) | 18 (85.7) | 4 (80) | 1 (20) | 10 (31.2) | 22 (68.8) |
| 6 | Presence of information dissemination tool for PV | 1 (16.7) | 5 (83.3) | 2 (9.5) | 19 (90.5) | 4 (80) | 1 (20) | 7 (21.9) | 25 (78.1) |
| 7 | Presence of safety database support | 0 (0) | 6 (100) | 1 (4.8) | 20 (95.2) | 4 (80) | 1 (20) | 5 (15.6) | 27 (84.4) |
| 8 | Presence of ADR reporting form in the company | 1 (16.7) | 5 (83.3) | 7 (33.3) | 14 (66.7) | 2 (40) | 3 (60) | 10 (31.2) | 22 (68.8) |
| 9 | Process in place for collection, recording, and analysis of ADR | 3 (50) | 3 (50) | 8 (38.1) | 13 (61.9) | 5 (100) | 0 (0) | 16 (50.0) | 16 (50.0) |

**Table 5:** Analysis of complementary structural Pharmacovigilance indicators in selected pharmaceutical companies, Addis Ababa, Ethiopia, 2020, (n=32)

| S/N | Complementary Structural Indicators | Response (N (%)) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *Local manufacturer* | | *Importer* | | *Multinational manufacturer* | | *Total* | |
| | | Yes | No | Yes | No | Yes | No | Yes | No |
| 1 | Presence of dedicated computers for PV activities | 0 (100) | 6 (100) | 0 (100) | 21 (100) | 3 (60) | 2 (40) | 3 (9.4) | 29 (90.6) |
| 2 | Presence of functioning and accessible communication facilities | 2 (33.3) | 4 (66.7) | 4 (19) | 19 (80.1) | 4 (80) | 1 (20) | 10 (31.2) | 22 (68.8) |
| 3 | Presence of reference sources for drug safety information | 2 (33.3) | 4 (66.7) | 5 (23.8) | 16 (76.2) | 4 (80) | 1 (20) | 11 (34.4) | 21 (65.6) |
| 4 | Organization of PV training for health professionals | 1 (16.7) | 5 (83.3) | 4 (19) | 17 (80.1) | 5 (100) | 0 (0) | 10 (31.2) | 22 (68.8) |
| 5 | Presence of source of data on consumption and prescription of medicines | 2 (33.3) | 4 (66.7) | 6 (28.6) | 15 (71.4) | 4 (80) | 1 (20) | 12 (37.5) | 20 (62.5) |
| 6 | Presence of SOP for RMP | 3 (50) | 3 (50) | 5 (23.8) | 76.2) | 2 (40) | 3 (60) | 10 (31.2) | 22 (68.8) |
| 7 | Presence of SOP for PSURs | 1 (16.7) | 83.3) | 3 (14.3) | 18 (85.7) | 2 (40) | 3 (60) | 6 (18.8) | 26 (81.2) |
| 8 | Training of staffs on RMPs | 3 (50) | 3 (50) | 4 (80) | 1 (20) | 5 (23.8) | 16 (76.2) | 12 (37.5) | 20 (62.5) |
| 9 | Presence of marketed products with RMP | 2 (33.3) | 4 (66.7) | 0 (0) | 21 (100) | 4 (80) | 1 (20) | 6 (18.8) | 26 (81.2) |
| 10 | Presence of reports that have been processed and sent to RA | 5 (83.3) | (16.7) | 15 (71.4) | 6 (28.6) | 5 (100) | 0 (0) | 25 (78.1) | 7 (21.9) |
| 11 | Sending of reports within stipulated company/RA | 5 (83.3) | (16.7) | 15(71.4) | 6 (28.6) | 5 (100) | 0 (0) | 25 (78.1) | 7 (21.9) |

This study found that similar to hospitals, the majority of the pharmaceutical companies in the study did not keep proper records for process-level PV indicators. As a result, it was impossible to obtain an exact figure for each process and outcome level PV indicator, and only the percentages of pharmaceutical companies that reported "Yes" or "No" but were unable to provide documented (recorded) data were narrated. For example, 14 (43.7%) pharmaceutical companies (0 local manufacturers, 13 importers, and 1 multinational manufacturer) reported receiving ADR in the previous calendar year but were unable to verify with recorded data. Furthermore, 13 (40.5%) pharmaceutical companies (2 local producers, 10 importers, and 1 multinational manufacturer) reported the presence of reports in their database but were unable to provide documentation. None of the pharmaceutical companies conduct active surveillance operations that began, continued, or ended in the previous five calendar years.

Most of the outcome indicators used did not apply to pharmaceutical companies. Therefore, such indicators are excluded from the analysis.

### 5.1.4. Pharmacovigilance at the level of National Regulatory Authority

The performance of EFDA about PV structure, process, and outcome indicators are presented in Tables 6, 7 & 8. Except for unavailability of regular budget and standard ADR reporting form for the general public, all other core structural requirements are fulfilled at the national level (Table 6). Library or reference for safety information, and web-based training tools are not available at the NRA.

**Table 6**: Analysis of core Pharmacovigilance structural indicators at the national regulatory authority of Ethiopia, Addis Ababa, Ethiopia, 2020

| S/N | Core Structure Indicators | Finding | | |
|---|---|---|---|---|
| | | **Yes** | **No** | **Remark** |
| 1 | Availability of statutory provision (national policy, legislation) for PV | √ | | Incorporated within the Proclamation |
| 2 | Presence of PV center or unit with standard accommodation | √ | | Organized as a separate directorate |
| 3 | Availability of regular financial provision (statutory budget) for the PV Centre | | √ | Considered with other budget plans of the authority |
| 4 | Presence of human resources to carry out functions properly | √ | | A mix of professionals in medicine, medical device, food, and laboratory |
| 5 | Presence of SOP for PV | √ | | SOP for receiving and processing ICSRs |
| 6 | Presence of national ADRs database | √ | | Directly adopted from WHO |
| 7 | Computerization (digitalization) of ADR database | √ | | Shared with WHO |
| 8 | ADR reports sent to the WHO database (Uppsala) | √ | | Reports with completed data |
| 9 | Presence of Publication of ADR bulletin (newsletter) by PV center | √ | | Newsletter published every 4 months (quarterly) |
| 10 | Availability of clear communication strategy for routine communication and crises communication | √ | | Fax, Email, website, Toll-free line (regularly promoted at 7.00 am on national morning radio broadcasting) |
| 11 | Presence of standard ADR reporting tool (form) | √ | | Both manual and electronic yellow form and mobile application (Med-safety) |
| | 11a: Presence of relevant fields in the standard ADR form to report suspected medication errors | √ | | Contain minimum information for reporting |
| | 11b:Presence of relevant fields in the standard ADR form to report suspected counterfeit/ substandard medicines | √ | | |
| | 11c: Presence of relevant fields in the standard ADR form to report therapeutic ineffectiveness | √ | | |

| | | | | |
|---|---|---|---|---|
| | 11d: Presence of relevant fields in the standard ADR form to report suspected misuse, abuse and/or dependence on medicines | √ | | |
| | 11 e:Availability of standard ADR reporting form for the general public | | √ | |
| 12 | Presence of mechanism in place for collection, recording, and analysis of ADR reports | √ | | |
| 13 | Presence of tools for PV information dissemination | √ | | PV Newsletter, website, email, phone |
| 14 | Availability of PV advisory committee or an expert committee in the setting capable of providing advice on medicine safety | √ | | Transformed the Adverse Event Following Immunizations (AEFIs) committee to a general safety advisory committee |

**Note:** √ shows the availability of the structural indicator

**Table 7:** Analysis of complementary Pharmacovigilance structural indicators at the national regulatory authority of Ethiopia, Addis Ababa, Ethiopia, 2020

| S/N | Complementary structure indicators | Finding | | |
|---|---|---|---|---|
| | | Yes | No | Remark |
| 1 | Availability of dedicated computer for PV activities | √ | | Used for recording and further processing of incoming reports |
| 2 | Availability of functioning and accessible communication facilities in the PV Centre | √ | | Website, E-mail, fax, toll-free phone |
| 3 | Availability of library or other reference sources for drug safety information | | √ | Free Internet access and online sources |
| 4 | Presence of computerized case-report management system | | √ | |
| 5 | Presence of program (including a laboratory) for monitoring the quality of pharmaceutical products | √ | | ISO/IEC17025/:2005 accredited laboratory for physicochemical & condom testing up to 2021 |
| 6 | Presence of essential medicines list which is in use | √ | | Latest updated in 2015 |
| 7 | Consideration of PV when developing the main standard treatment guidelines for the country | √ | | |
| 8 | Organization of training by PV Centre for health professionals | √ | | 2-3 days training on ADRs & separate training for AEFIs (for 20-40 attendees per session) |
| 9 | Availability of web-based PV training tools available for health professionals & public | | √ | |

| | | | | |
|---|---|---|---|---|
| 10 | Presence of requirements mandating MAHs to submit periodic safety update reports | √ | | Not enforced (Self-initiated by MAH) |
| 11 | Presence of regulatory decision based on local PV data in the last 2 years | √ | | Withdrawal, restriction on use and warning letter |
| 12 | Presence of mechanism for the provision of feedback to reporters | √ | | Using email & prepaid post |

**Note:** √ shows the availability of the structural indicator

As it is depicted in Table 8 below, the NPC under EFDA exercises some of process indicators such as receiving and recording of reports, conducting causality assessment and conducting PMS activities.

**Table 8:** Analysis of core Pharmacovigilance process indicators at the NRA, Addis Ababa, Ethiopia, 2020

| S/N | Core Process Indicator | Result | Remark |
|---|---|---|---|
| 1 | Total no of ADR reports received in the previous year | 1416 | 1329 ADR, 87 product quality defect |
| 2 | Current total no of reports in the RA's database | 4019 | Total no of report during data collection |
| 3 | Percentage of total reports acknowledged/issued back to reporters | 100 | Using either email or post but not sure whether it is reached or not to a reporter |
| 4 | Percentage of total reports subjected to causality assessment in the past year | 2 | Only conducted for serious ADEs. 2 serious ADEs/800 total reports. |
| 5 | Percentage of total annual reports satisfactorily completed and submitted to the national PV center in the previous year | - | No documented data |
| 6 | Percentage of reports of therapeutic ineffectiveness received in the last year | 1 | 1/800 reports |
| 7 | Percentage of reports on medication error reported in the previous year | 0 | Not frequently detected and reported |
| 8 | Percentage of registered pharmaceutical companies that have functional PV system | 0 | |

| | | | |
|---|---|---|---|
| 9 | No of active surveillance activities are or were initiated, ongoing or completed in the past five years | 03 | Cohort event monitoring (CEM) on ARV medication, HPV vaccine |

**Table 9:** Analysis of complementary Pharmacovigilance process indicators at the NRA, Addis Ababa, Ethiopia, 2020

| S/N | Complementary Process Indicators | Result | Remark |
|---|---|---|---|
| 1 | No of face to face training conducted on PV in the previous year for health professionals | 20 | Number of health professionals trained not known |
| 2 | No of face to face training conducted on PV in the previous year for the general public | 0 | |
| 3 | No of registered products with PV plan or risk management strategy from MAHs in the country | 0 | |
| 4 | Percentage of MAHs submitting PSURs to the regulatory authority as stipulated in the country | No documented data | Not enforced by the RA and submission of PSURs is by the companies' self-interest |

As indicated in table 9 above, the regulatory authority conducted few trainings to professionals but couldn't perform face to face training for the general public and no data on PSURs submitted to NRA. In addition, as observed in table 10 below the authority didn't have documented data on no signals generated in past 5 years by the center and percentage of preventable ADRs

**Table 10:** Analysis of core Pharmacovigilance outcome indicators at the NRA

| S/N | Core outcome Indicators | Finding | Remark |
|---|---|---|---|
| 1 | Total no of signals generated in the past 5 years by the PV Centre | - | No documented figure |
| 2 | No of regulatory actions taken in the preceding year | 4 | |
| | 2a: Product label changes (variation) | 0 | |
| | 2b: Safety warnings on medicines to | 1 | |
| | 2c: Withdrawals of medicines | 2 | |
| | 2d: No of other restrictions on the use of medicines | 1 | |
| 3 | Percentage of preventable ADRs out of the total number of ADRs reported in the preceding year | - | No documented data |

**Table 11:** Analysis of complementary Pharmacovigilance outcome indicators at the NRA

| S/N | Complementary Outcome Indicators | Finding | Remark |
|---|---|---|---|
| 1 | Percentage of medicines that are counterfeit/substandard/in the pharmaceutical market | - | No documented data |
| 2 | No of analysis report published in the last two years | 0 | The majority has done by UMC |
| 3 | No of reports that have been submitted to UMC in the last two years | 320 | |
| 4 | No of products voluntarily withdrawn by MAHs because of safety concerns in last year | 0 | Mostly done by RA |

## 5.2. Qualitative Study

### 5.2. 1. Socio-demographic characteristics of Key Informants

A total of 22 KIs aged between 25 and 65 years were interviewed. Regarding their work area, 8 were from pharmaceutical companies, 9 from hospitals, and 5 from the NRA. The detailed socio-demography of the KIs is presented in Table 12.

**Table 12:** Socio-demographic characteristics of key informants (n=22)

| Characteristics | Category | N (% ) |
|---|---|---|
| Gender | Male | 14 (63.6) |
| | Female | 8 (36.4) |
| Age group (years) | 25-30 | 3 (13.6) |
| | 31-35 | 10 (45.4) |
| | 36-40 | 5 (22.7) |
| | ≥40 | 4 (18.2) |
| Academic qualification | Bachelor's degree | 7 (31.8) |
| | Master's degree | 15 (68.2) |
| Profession | Pharmacist | 22 (100) |
| Work experience (years) | 5-10 | 6 (27.3) |
| | 11-15 | 12 (54.5) |
| | ≥16 | 4 (18.2) |
| | Hospital pharmacy head | 8 (36.7) |

| | | |
|---|---|---|
| Work Position | Medical representative | 2 (9.0) |
| | Manager (General, Deputy, or/and Technical) | 3 (13.6) |
| | Directorate director (EFDA) | 3 (13.6) |
| | Inspector | 1 (4.5) |
| | Quality assurance and regulatory affairs officer | 3 (13.6) |
| | PV Coordinator | 1 (4.5) |
| | Drug information service head | 1 (4.5) |
| Work area | Pharmaceutical companies (importer, local and multinational manufacturers) | 8 (36.4) |
| | Hospital (Government and Private) | 9 (40.9) |
| | National Regulatory Authority | 5 (22.7) |

### 5.2.2. Experiences and opinions of key informants on Pharmacovigilance implementation

A manual thematic analysis was followed for analysis and interpretation of results under four core thematic categories through both inductive and deductive approaches. The four major themes were: Perception of current PV status; factors influencing the implementation of PV; impacts of PV on the healthcare system; and suggested strategies for effective implementation of PV. Under the four majors themes, eleven subthemes were identified described below.

**Theme 1: Perception of current Pharmacovigilance status**

During the interview, KIs provided their view about the overall PV system, current practices, and status in the country. Accordingly, the majority of them rated and characterized the country's PV system as weak, isolated, uncoordinated, and loose, focused on reactive approach, remained on paper and found at the infancy stage. This was substantiated by the following accounts from two informants:

> *For me, the pharmacovigilance system in the country is at the very infancy stage and it is not well-practiced. Even though the regulatory authority prepared and passed different regulations, guidelines, directives, and working standards, it is*

*not well implemented and remains on paper.[P5, General Manager, 37 yrs.' Experience, Import]*

*[…] Overall the system is still young and reactive. It seems just a one-time campaign rather than continuous vigilant activity. When there are certain safety-related problems, the regulatory authority responds to that particular problem. It is just working like to 'put off the fire'. [P8, Medical representative, 7 yrs.' Experience, Multinational manufacturer]*

KIs also compared the PV system of the country with other developed and some developing countries and cited that the PV system in Ethiopia is comparatively weak and is not working in a way as it should be. They characterized the PV system as a system with a lack of trained professionals in the field, centralized activity at the NPC, lack of commitment from stakeholders, lack of awareness from health professionals, lack of communication among stakeholders, and lack of proper implementation. This was strengthened by the following account.

*[…]It requires strengthening the system in terms of an expert in the field, training, and automation. It also requires the collaboration and communication of all stakeholders including manufacturers, importers, distributors, retailers, health professionals, and regulatory* authority. *[P7, Regulatory Affairs and Quality Assurance Expert, 6 yrs.' Experience, Import]*

In contrary to the above reflections, few respondents described the current PV system in the country is good compared with some African countries by mentioning some of the activities of the RA. They indicated that the RA tries to conduct PMS on targeted products, control custom entry points and take samples for further quality tests, accept reports from different sources and send to the UMC. They also declared that there is a commitment from the government on the issue including the ministry of health corroborating their claim as follows:

*[…] As a country, we have an idea. For example, the regulatory authority tries to conduct PMS, control custom entry points, and accept reports from different sources. But, these activities need further development and expanded to protect patients and the pharmaceutical market. [P11, Management, 12 yrs.' Experience, Regulatory Authority]*

**Theme 2: Factors influencing the implementation of Pharmacovigilance**

Another main theme that emerged from the qualitative analysis was the factors that limit the effectiveness of the PV system in the country. KIs identified some of the main factors and categorized them under two general sub-themes as resource-related and reporting-related.

**a. Resource Related Factors**

During the interviews, resource constraint was frequently mentioned by the majority of the respondents as the main contributing factors that have an impact on the overall functioning of the PV system in the country. Finance, personnel, technical capacity, and legal/political support were cited as the most important ones in this regard.

***Human resource***

KIs indicated that an adequate number of qualified and experienced professionals is a foundation for building and running a robust PV system. However, the majority of the participants mentioned that there is a lack of adequate number, appropriately trained and skilled expertise in the area further compounding the challenges to smoothly run the PV system. This was reinforced by the accounts from the KIs:

*[…]As a country we don't have adequately trained professionals in pharmacovigilance. There is no assigned personnel at manufacturers, importers, and hospitals level who are responsible for managing medicine safety issues. [P5, Deputy General Manager, 12 years experience, Local manufacturing]*

> […] *There is a lack of experienced manpower in this particular area compared to developed countries that have well-trained professionals in the field of pharmacovigilance. [P2, Regulatory and QA personnel, 12 yrs.' experience, Local Manufacturing]*

As clearly cited by KIs, the shortage of qualified PV staff resulted in unintended consequences such as poor detection of medicines' adverse effects, inadequate capacity to understand, assess, prevent, and manage safety-related risks. In this regard, informants also indicated that the NRA (NPC) lacks safety data analysis expertise and unable to take sound local regulatory decisions.

> *We use the WHO method for causality assessment but there are times that we are unable to analyze by ourselves due to a lack of experts in the area. As a result, we would be forced to send most of the incoming safety reports to Uppsala Monitoring Centre without doing any analysis. [P 18, Management, 12 yrs. Experience, Regulatory Authority]*

***Funding for PV system***

Most of the KIs identified financial constraints as an important challenge for PV-related activities in their respective organizations, and in the country. It was also reported that their respective organizations do not have a dedicated budget for PV system implementation as substantiated by the following account taken from one of the informants:

> *I think we don't have a problem with the legal framework. What we really lack is an appropriate fund to run the Pharmacovigilance system smoothly. [Participant, 4, Manager, 37 yrs.'' experience, Import]*

They further explained that lack of a dedicated budget for PV, incapacitates the PV centers, hospitals, pharmaceutical companies, public health programs, and the NPC undertake key activities including ICSRs collection, conducting active and passive surveillance activities,

requisite and regular staff training, and limit the capacity to expand PV centers to other parts of the country. In addition to the NPC, pharmaceutical companies, and health facilities cannot conduct some of the PV-related activities such as organizing PV units equipped with necessary facilities, technology, and manpower, and continuous awareness creation to their staff, health professionals, and patients.

> *Even though the regulatory authority is committed to Pharmacovigilance, there is a lack of funding to the program from the government side; consequently, the central pharmacovigilance center may not execute its work effectively. [P7, Regulatory Affairs and Quality Assurance Expert, 6 yrs.' experience, Import]*

***Social resources***

Concerning social resources, KIs identified some of the components of social resources including collaborations, cooperation, partnership, and communication among resource-related constraints manifested in the country's PV system. It was stressed that the existing weak relationships, disengagement, and uncoordinated communication among key stakeholders including the RA, health facilities, pharmaceutical companies, public health programs, and society are critical issues calling for strategic intervention. This was supported by the following statements:

> *There is weak inter-institutional communication and collaboration. The relationship between the central regulatory authority with regional regulatory bodies, the communication and information exchange between pharma companies and hospitals with the regulatory authority still requires further improvements. [P9, Deputy Manager, 37 yrs. experience, Local manufacturing]*

*[…] There is also a lack of communication between us (pharmaceutical companies) and authority. [P7, Regulatory Affairs and Quality Assurance Expert, 6 yrs.' experience, Import]*

Besides, KIs indicated that most reports coming to the NPC (RA) are from medical institutions, mainly from hospitals. Compared to reports coming from health institutions, the reporting from pharmaceutical companies is less. The pharmaceutical companies don't have well-structured PV practices to safeguard patients and the communities from harm that may be resulted from their marketed products.

***Materials (Technical resources)***

Inadequate technical resources such as lack of data analysis and communication tools, data management infrastructure (database), accredited testing laboratories, and reporting tools, were among the mentioned resource-related constraints.

KIs commented on the unsuitability of the present paper-based reporting form citing that it is resource-intensive and results in duplication of efforts. And could not encourage HCPs to fill the form and report even though they identify ADR. This was accounted for by the following opinions from the KIs:

*[…] The paper form reporting is not available everywhere and even not suitable to report. This may be due to its cost implication in the printing and distribution process. [P8, Medical representative, 7 yrs. Experience, Multinational]*

*It is a long time since I have seen the ADR form in our setting. Sometimes the authority does not distribute the form to us. Even they do not check its availability. [P20, Hospital pharmacy head, 10 yrs.' Experience, Hospital]*

Another technical related resource mentioned by few respondents was the shortage of quality testing laboratories in the country. The number of well-equipped, accredited, and properly

functioning laboratories is few compared to the increasing demand to check the quality of the product in the country. Due to limited capacity in quality control laboratories, it has not been possible to conduct mass testing of available products in the market to check their quality and pass timely regulatory action as substantiated by KIs account.

> *We don't have adequate certified laboratories. As a country, we have only one laboratory located at the regulatory authority. We cannot able to test all samples to check whether they are standard or counterfeit when ADRs and other quality issues are reported. [P22, Technical Manager, 8 yrs.' experience, Import]*

***Political and legal support***

Some participants mentioned that lack of adequate legal infrastructure played a prominent role for the presence of weak medicine safety monitoring systems in the country. Some of the reported factors in this regard include weak law regulatory enforcement practice, inability to prepare separate PV-specific policy, inaccessibility of legal instruments to respective stakeholders, and inability to timely provide feedback and executive measures to reports from the industry and HCPs.

The KIs stressed that the enforcement capacity of the authority is not adequate. Even though the PV guideline clearly states the responsibility of pharmaceutical companies in reporting and managing safety-related issues of their products, there is a lack of enforcement regarding mandatory reporting and submission of PSURs from pharmaceutical companies. They also emphasized that without mandatory requirements for ADR reporting, PSURs, and PMS from pharmaceutical manufacturers, the PV target is missed; and this was corroborated by the following accounts.

> *[…] The regulatory authority is less stringent. Most of the time, the authority does not enforce and control pharmaceutical companies to have Pharmacovigilance units,*

*qualified persons for pharmacovigilance, and other safety management systems.[Participant 11, Management, 12 yrs. experience, Regulatory Authority]*

*Even though, pharmacovigilance (PSURs) report is mandatory to the market license holder, (MAHs), the regulatory authority does not ask and enforce you to submit the periodic safety update report. [P6, Regulatory Affairs and Quality Assurance Expert, 6 yrs.' experience, Import]*

In contrast, few respondents acknowledged the political commitment of the RA and government on PV. They related the current activities of the authority to expand the existing PV activities by mentioning some positive experiences such as the expansion (decentralization) of PV centers to different teaching hospitals in the county, organization of PV unit as an independent directorate, increasing the professional mix of the NPC, starting alternative methods of reporting tool (mobile Med-Safety ADE reporting application) and negotiation of the authority with the ministry of finance on the separate budget agreement for the NPC. This was supported by the following accounts from respondents.

*Previously, there was a pharmacovigilance unit under the registration and licensing directorate with one focal person. Currently, it is organized as an independent directorate and separate staff with diverse professionals are assigned for pharmacovigilance and clinical trial to give special emphasis to pharmacovigilance. [P15, Management, 10 yrs.' experience, Regulatory authority]*

*[…] The authority started opening different pharmacovigilance centers in different universities teaching hospitals and these centers are assumed to coordinate and strengthen the pharmacovigilance activities in the country. It is also planned to expand (decentralize) the pharmacovigilance center to other additional hospitals in the country. [P17, Management 12 yrs.' experience, Regulatory authority]*

**b. Reporting Related Factors**

Issues related to reporting were other contributing factors addressed by the majority of the respondents as manifested by the weak PV implementation in the country. To this end, low health professionals' knowledge and awareness and shortage of reporting formats were frequently raised.

***Health professionals' knowledge and awareness***

The majority of informants declared that health professionals are among the main stakeholders who play an important role in PV and ensuring patient safety in terms of identification (detection), assessment and reporting of ADR, and any medicine safety issues. To this effect, HCPs' knowledge and awareness of PV have a significant contribution. In Ethiopia, despite available tools to report ADRs, the PV system is not well understood by most health professionals. The presence of inadequate knowledge, wrong perception about reporting, and low-level awareness of health professionals towards PV were frequently mentioned by most informants as the main manifestation of the low reporting rate in the country. This was witnessed by the following accounts.

> *To identify, assess, report, analyze ADR and send report to the concerned body, it requires knowledge, awareness, and consciousness. In our country, there is a low level of awareness and negligence from the health professional's side. The ADR reporting form may not properly be used and filled by professionals. They also perceive that reporting is not important and regulatory authority may not take action. [P16, Inspector, 7 yrs. Experience, Regulatory Authority]*

> *Health professionals have low awareness of reporting and give less priority to PV. For example, most health professionals neglect many unintended reactions by considering it as a common side effect. This clearly shows the presence of a gap in knowledge about*

*what is to be reported or not. [P19, Drug Information Service Head, 9 yrs. Experience, Hospital]*.

***Reporting tools***

The way reporting of ADR and other medication safety issues has a huge impact on the success of the final report submitted to the RA. Participant experts indicated that the RA has introduced reporting tools to report ADR cases such as the manual (paper-based) prepaid reporting form, email account, free -Toll, and recently introduced mobile application (Med-Safety). Despite this, most respondents stressed the weakness of the current reporting mechanisms as the manual reporting tool is not regularly distributed, cumbersome (take time to fill and send), and is not easily accessible to reporters. Respondents from a few hospitals and pharmaceutical companies indicated that the ADR reporting form is not available in their setting.

*The currently available ADR reporting form is tedious and time taking to fill and send. […]. Also, the paper form of the reporting card is not available everywhere. [Participant 10, Technical manager, 12 yrs. experience, Multinational]*

*Theoretically, there is an ADR reporting form but not well distributed throughout the country. For example, the yellow form is not available in our hospital and is not collected regularly to generate data and communicated on time. [P7, Regulatory and Quality Assurance Expert, 6 yrs. experience, Hospital]*

Besides, respondents expressed that the authority launch ADE reporting mobile application which enables to report to the RA, and this would simplify and eliminate the drawbacks of the manual (paper) reporting form. Even though this new mobile application is launched, it requires a smartphone, internet, proper promotion, advocacy, and sensitization to health professionals and the public in general as supported by the following statement.

*[…] The new mobile Med-Safety reporting system will work in the presence of the internet and smartphone. Due to this, reporters may not use it. Therefore, it would be effective if it made offline and applicable to all reporters. [P15, Management, 10 yrs. experience, Regulatory Authority]*

**Theme 3: Impacts on the healthcare system**

An inefficient and uncoordinated national PV system will have different consequences on the entire health care system. Participants identified some pertinent consequences that will be resulted from a weak and inefficient PV system. Compromising patient's quality of care, feeling of insecurity and loss of confidence, increased circulation of unsafe product, economic impact, and cost implications were among the commonly stated consequences.

**a. Compromising patient's quality of care**

Concerning patients' quality of care, the majority of the respondents expressed that the absence of an appropriate PV system in the country will expose patients to unnecessary harm and patients' quality of care will be compromised which finally endangers the entire health system. This was further strengthened by the following statement.

*Supply of pharmaceutical products without a proper vigilance system may end up with patient harm rather than the benefit and the community will be adversely harmed by those medications taken for their medical condition. [P2, Regulatory and Quality Assurance Personnel, 12 yrs.' experience, Local Manufacturing]*

**b. Feeling insecurity and loss of confidence**

In addition to a patient being harmed, KIs stated that the presence of frequent medicine safety concerns in the country may result in a feeling of insecurity and loss of trust and confidence by patients and the society on the government and the regulatory body. Consequently, patients and the public may develop fear towards using medicines in the time of need for treatment, and

finally, the health care system of the country may fall at risk. One informant stated the condition as follows.

> *In a society where there is distorted perception about medicines circulating in the market, they may consider that unsafe and low-quality medicines are dispensed to them because the regulatory authority failed to do its job properly. This eventually may erode public trust and confidence in the authority and in the health care system of the country. [P11, Management, 12 yrs. 'experience, Regulatory Authority]*

Also, some respondents added that countries that trade pharmaceuticals with Ethiopia, may lose confidence and ban exporting their products to Ethiopia and drop their investment in the pharmaceutical sector. The following statements from respondents strengthen this.

> *[…] Pharmacovigilance is a global agenda that requires the collaboration of the world. If we don't have a well-functioning Pharmacovigilance system as a country, the image of the country regarding medicine safety will be under question. [P4, Manager, 37 yrs. experience, Import]*

**c. Economic impact and cost implication**

Concerning economic impact and associated costs, most KIs indicated that medicines are not only an essential component of health care but also an asset to the country's economy. It has an impact on the overall economy of the country as medicines account for the highest expenditure in the county's health budget. In addition to unintended costs incurred due to poor PV system, other indirect costs including the withdrawal of medicines with safety concerns may impact the national economy as was corroborated by key informants.

> *If the safety of medicines is compromised, the country will lose benefits from the imported products and leads to additional costs to treat the affected individuals. [P20, Hospital Pharmacy Head, 10 yrs.' experience, Hospital]*

### d. Increased circulation of unsafe products

Some respondents indicated that the absence of a strong PV system may encourage the circulation of counterfeited and substandard products in the country. The presence of such products on the market might come due to a lack of traceability and lead to an unhealthy market in the pharmaceutical sector. As a result of weak PV and regulatory systems (inadequate auditing and inspection) by the authority, those individuals or groups who are involved in the circulation of the counterfeit product will be encouraged and flourished and legal suppliers will be affected.

> *[…]In our country, different products are assumed to be counterfeit and substandard. We don't have clear track and trace mechanisms to identify such medicine safety-related rumors. [P10, Technical manager, 12 yrs. experience, Import]*

> *[…] Products with compromised safety and efficacy will affect the entire pharmaceutical market in the country through discouraging legal business firms and encourage the flourish of illegal ones and promote bad practices [P17, Management, 12 yrs.' experience, Regulatory Authority]*.

## Theme 4: Suggested strategies for effective implementation of PV

Concerning improving mechanisms for the present PV system, seven strategies were identified by the KIs as summarized below:

### a. Systems-related strategies

Participants identified some system-related ways to improve the existing challenges in the country's PV system.

Among system-related mechanisms, integrating clinical care of patients with the national activity PV activities was suggested as one of the strategies. To this effect, reporting ADR and other medicine safety problems as part of the HCPs' daily routine clinical practice and linking

to the performance appraisal of the healthcare workers was mentioned as an important strategy, and this was substantiated by the following account.

> *[…] Every HCP who is involved in the provision of clinical care to the patient needs to be required to report ADRs and this can be as one part of the evaluation of the health professionals. [P19, Drug Information Service Head, 9 yrs. experience, Hospital]*

The other commonly cited system-related improving mechanism was expanding (decentralizing) the centralized PV center to the different parts of the country. Respondents indicated that the current PV is centralized and requires decentralization to different health institutions.

> *Ethiopia is a vast country, having only one national Pharmacovigilance center for coordinating all the pharmacovigilance activities in the entire country could be a very challenging task. Therefore, this requires decentralizing the center to other parts of the country. [P21, Pharmacovigilance and Clinical Trial Coordinator, 10-year experience, Regulatory Authority]*

Respondents also provide their critiques regarding the inclusiveness of the current reporting platforms in Ethiopia. Accordingly, the current reporting platform is claimed as professional centric and it doesn't allow reporting by patients. The KIs underscored the inclusion of patient/consumer reporting format which enables the RA to get full information and also further enrich reports coming from professionals. Patient reporting allows increased understanding, early detection of safety issues, and taking the necessary action, as it was substantiated by one KI's account.

> *[…]. We don't have a patient reporting format and even it is not expected to report. Therefore, we (Regulatory authority) are working to incorporate these gaps.[P15, Management, 10 yrs. experience, Regulatory Authority]*

Also, respondents revealed that the current reporting tool is not user-friendly and the implementation of easy, user-friendly, and accessible reporting tools was suggested as an important option. Among the suggested reporting tools, offline electronic reporting, and other digital platforms were indicated.

> *[…] The reporting form is not easily accessible and time taking to duplicate and send back to the regulatory authority through a post. Therefore, there should be an automated online reporting system to facilitate (modernize) the reporting. [P4, Manager, 37 yrs. experience, Import]*
>
> *The newly implemented mobile Med-safety reporting system works in the presence of the internet and smartphone. Due to this, many people may not use it. Therefore, it would be effective if it is offline and applicable to all reporters. [P14, Hospital DIC Head, 30 yrs. experience, Hospital]*

**b. Improving the regulatory system and capacity**

KIs indicated that one of the key reasons behind the limited implementation of PV is the inadequate enforcing capacity of the existing regulation and lack of PV-specific policy. Supporting the current regulation by establishing PV-specific policies addressing PV activities was suggested as a measure that can help to integrate the PV systems. Even though the present PV guideline indicates the responsibility of each stakeholder, the ability to act, implement, and enforce RA is less. The present PV guideline states that pharmaceutical companies (MAH) have to report any product-related problems, submit PUSRs, and conduct PMS, but the authority does not enforce them to implement. In addition to pharmaceutical companies, incorporating regulation/guidelines for patient reporting and making reporting mandatory by health professionals were among the mentioned regulatory-related strategies. The following statements show the personal opinions of two KIs:

*As the main stakeholder, the regulatory authority should work on enforcement. The authority should work on controlling and overseeing the pharmacovigilance activities of pharmaceutical companies and health facilities. [P10, Technical manager, 12 yrs. experience, Import]*

*[…] One of the key activities should be working on the regulation part. Enforcing of market license holders to follow the safety profile of their products is very important. This can be done through support by regulation. For example, enforcing them to have QPPV and making the reporting system mandatory for health professionals. [P15, Management, 10 yrs. experience, Regulatory Authority]*

**C. Training and advocacy: Boosting of knowledge and awareness**

Reporting of ADR and other medication safety issues is the backbone of PV. Successful reporting primarily relies on knowing the role of reporting and its positive impact on public health and clinical practice. HCPs are central for the identification of new concerns on the safety and effectiveness of medicines. If HCPs are trained and sensitized to appreciate the contributions AEs reporting, it may help to stimulate interest in PV. KIs suggested that creating awareness and boosting knowledge among HCPs and the community at large was among the possible ways to improve reporting. Addressing PV in relevant curricula, conducting a continuing professional development course on PV, or in-service training were suggested as important strategies.

### d. Motivation of reporters

Implementation of different incentive schemes such as the provision of quick feedback and acknowledging reporters was suggested by a few respondents as an incentive. In this regard, the provision of quick response and the actions taken on the status of the report, and recognition of best performers in specific health settings can be an incentive for healthcare workers to

report identified ADRs and other medicines safety issues. This was strengthened by the following accounts.

> *[…] I advise the provision of feedback to the individuals who are involved in reporting what happened after he/she has reported advantageous. It enables reporters to see their impact and they will be encouraged to report more and may motivate the morale of the reporter and make them feel good about what they are contributing. [P12, Medical Representative, 8 yrs. experience, Multinational Manufacturer]*
>
> *[…] Reinforcing the reporters is important though reporting of ADR and any safety issue is their professional duty. Also, the presence of a mechanism that allows reporters to know the status of their report and any regulatory actions made is critical. [P19, Hospital DIC Head, 30 yrs. experience, Hospital]"*

**e. Increasing stakeholders' engagement and communication**

To build a strong, full-fledged, and sustainable national PV system, it is necessary to engage different actors that have a crucial role in sustaining the system. The majority of the respondents added that there is a lack of participation, coordination, communication, collaboration, and partnership among responsible stakeholders such as RA, pharmaceuticals companies, public health programs, health professionals, and health facilities. Active engagement and creating strong partnerships among relevant stakeholders were mentioned as a positive move and will have a critical role in the proper functioning of the PV system in the country. It was also indicated that the presence of effective communication among the stakeholders is vital to operate for the best benefit of the patients and to make timely regulatory decisions. This was witnessed by the following accounts.

*[…] There is a lack of communication between us (pharmaceutical companies) and authority and this a gap. PV requires active reminders and engagement. [P7, Regulatory and Quality Assurance Expert, 6 yrs. experience, Import]*

*[…] Health professionals and pharmaceutical companies may not know the presence of ADR reporting forms. To this effect, the regulatory authority neither provides us any training nor is reporting form to our company and our relationship is not that strong. This should be strengthened. [P3, Quality Assurance Manager, 12 years experience, Local Manufacturing]*

Participants also indicated that the best-designed PV system may not be worthy without the contributions of patients/consumers to provide information about the medicine and any potential impact on safety. To this end, some of the respondents stressed that the patient is marginalized in reporting ADR. Involving the community through the provision of information using a different communication channel was mentioned as a way to create awareness and improve patient reporting. This was supported by the following statement.

*[…] Similarly, we (Regulatory authority) don't have a patient reporting format and even it is not expected to report. Therefore, we should work to incorporate these gaps [P15, Management, 10 yrs. experience, Regulatory Authority]*

Besides, pharmaceutical companies were assumed as important stakeholders in extending the frontiers of PV within the country, engaging and mandating them to liaise with health practitioners/entities they serve was suggested as a way of improving the PV. It was indicated that the involvement of local companies in fulfilling their commitment to PV is less compared to foreign multinational companies who are operating in the country. This was witnessed by the following statements.

*Some foreign pharmaceutical companies review the safety of their products and submit periodic safety update reports to the regulatory authority. Such kinds of exercise are not seen by local manufacturers. The government has a plan to expand this to the local pharmaceutical sector. Therefore, local and foreign companies should work on improving their PV system. [P16, Inspector, 7 yrs.' experience, Regulatory authority]*

*[…] Once a product is out from your company, only a manufacturing document will remain with you. But, until the product expiry, we have full responsibility to follow its safety. We do this not only for the sake of pharmacovigilance but also for the survival of our company in the pharmaceutical market. [P4, Manager, 37 yrs. experience, Import]*

Few respondents also revealed that there are less integration and active collaboration of the country's PV system with public health programs, research, and medical institutions found in the country. It was indicated that the effectiveness of the PV system depends on a close relationship with these important partners. To this end, the authority is working with the ministry of health to integrate these public health programs with the PV system. Also, the NPC is working with different research and medical institutions that have active cohort event monitoring centers in the country. The following account strengthens this claim.

*[…] currently, we (regulatory authority) are also working on integrating our system with other stakeholders such as medical institutions, pharmacovigilance centers and universities. Besides, the regulatory authority has collaborations with research institutions like AHRI and TB programs. So, the presence of such collaborations strengthens the entire pharmacovigilance system. [P15, Management, 10 yrs. experience, Regulatory authority]*

# 5. Discussion

This study attempted to assess the PV system, current status, practices, and activities of hospitals, pharmaceutical companies, and the NRA. It also tried to identify their challenges and improving strategies.

The quantitative and qualitative findings of this study indicated that the PV system in the studied hospitals and pharmaceutical companies was found to be below the expected level of performance. Important core and complementary structural, process, and outcome PV indicators were not in place in the majority of hospitals and pharmaceutical companies. From the 30 hospitals included in the study, only one hospital (1 in 30) had a PV unit with a dedicated budget (3.3%), staff assigned (10%), information dissemination tool for PV, SOP (23.33%) for PV. These indicate that important structural elements are deficient in the majority of hospitals. The PV situation in this findings is much lower than the findings reported in five Asian countries where less than 50% of them had a PV center or unit, or dedicated staff for PV-related activities within their setting (Nwokike *et al.*, 2013). Another study's finding concurred with the present result (Abiri, O.T & Johnson, W.C.N, 2019).

Most of the complementary indicators such as the presence of dedicated computer and training for PV-related activities, having functional communication facilities, processing, and sending reports to the RA are not in place in the surveyed hospitals. This is consistent with other comparative analysis of PV systems study conducted in five Asian countries and an evaluative case study in Burkina Faso (Nwokike *et a*l., 2013; Kabore *et al.*, 2013).

To ensure good PV practices, it is essential to have good documentation practice with complete and up-to-date documentation and recording. It was observed that there was a lack of good recording and documentation practices in pharmaceutical companies, hospitals, and NPC. There was a lack of properly recorded and documented data in the hospitals showing that the

status of PV activities is low. Even though the hospitals declared the presence of process and outcome-related PV activities, it couldn't be retrieved and verified with documented evidence. For example, 17 (56.67%) hospitals declared that they had ADR that was identified in the last calendar year, 8 (26.67) indicated there were reports compiled and submitted to the PV center but could not objectively account for the claim. A study conducted at Hiwot Fana Specialized University Hospital, Harar, Ethiopia indicated that only 37.3% of HCPs recorded ADR in the patient follow-up chart indicating the poor practice of ADR documentation among HCPs (Shanko and Abdela, 2018). Another study conducted in six health facilities of Nigeria showed a lack of recording and documentation of ADRs (Opadeyi *et al.*, 2018; Olowofela, 2018).

Similar to hospitals, the majority of pharmaceutical companies included in the study showed deficiencies in performances in most of the core and complementary structure, process, and outcome PV indicators. For example, from a total of 32 companies included in the study, only 4 (12.5%) of them had separate PV unit, 12 (37.5%) had a regulatory unit, 5 (15.6%) had a regular budget for PV, 4 (12.5%) had dedicated staff for PV related activities and 10 (31.2%) of them had SOPs for processing ICSRs, PSURs or training of staff in PV, 12 (37.5%) companies provide training on RMPs to their staffs. A study conducted in pharmaceutical companies in Nigeria indicated similar findings (Nwaiwu *et al.*, 2016).

Alike to hospitals, most pharmaceutical companies lack most of the process and outcome/impact indicators. It was observed that most companies have poor record-keeping and documentation practices. As a result, most process and outcome/impact PV activities and results were not documented. Besides, the majority of the companies do not exercise most of the process and outcome level PV activities and practices. There is a lack of data on each process and outcome indicators to show the extent of PV activities and measure the final effect/result of the PV system of their company. As a result, it was possible to retrieve most of

the quantitative data from process and outcome PV indicators. A study conducted in LMICs showed deficiencies regarding process and outcome indicators (Olsson *et al*., 2010).

In contrary to pharmaceutical companies and hospitals, the NPC located under the NRA has basic infrastructure and procedures for PV-related activities. The NPC established under the NRA organized its basic PV infrastructures, such as establishing NPC with clear mandate, roles and responsibilities, formal organizational structure, dedicated staffs for PV, presence of functional information and communication infrastructure, PV guideline, PV SOP, safety bulletin (PV newsletter), medicine safety advisory committee and collaboration with the UMC. However, there is a lack of defined annual budget for PV, lack of data on consumption and/or prescription of medicines, no web-based training, and a lack of standard reporting form for the public. A comparative study conducted in four East African countries on the national PV system revealed a similar result (Barry *et al.*, 2020).

Even though the country has regulatory provisions that deal with organizational PV systems, its effectiveness depends on the availability of a sustainable budget and qualified staff. The NPC under the NRA does not have a sufficient regular budget. A review done by Isah *et al* (2012) in other African countries found similar results. Another comparative study done in four east African countries including Ethiopia, Kenya, Tanzania, and Rwanda indicated that Ethiopia and Rwanda do not have such a budget (Barry *et al.*, 2020). The study result also indicated that only one hospital had a budget for PV, and only 5 pharmaceutical companies had financial provisions for PV activities. A similar study done in five Asian countries showed a similar result (Biswas, 2013). As a result, a lack of dedicated PV budget, procedures, and training for HCPs resulted in a lack of capacity to consistently address PV issues. This is in line with a study conducted in Uganda, South Africa, and India (Maigetter *et al.*, 2015).

The qualitative exploration identified some of the contributing factors for the presence of ineffective and inefficient PV systems in the country citing resources constraint and issues

related to reporting as important contributing factors. Among these, shortage of qualified personnel, finance, technical expertise, legal/political commitment, and stakeholder engagement was repeatedly mentioned. This is comparable with other studies done in African countries (Olsson *et al*., 2010; Isah *et al*., 2012; Elshafie *et al*., 2018b).

Concerning human resources, it was indicated that the country didn't have adequate trained manpower on PV. None of the hospitals and pharmaceutical companies don't have qualified staff on PV. Also, the NPC is challenged by a lack of well-experienced and qualified expertise. As a result, the NPC is unable to conduct causality assessments for most of the incoming reports and is compelled to submit them to the WHO database. In a publication in the WHO's World Medicines Situation series by Pal *et al*. (2011), it was indicated that most national centers in developing countries were severely understaffed and under-resourced and most of their PV agenda is very much donor-driven

The success or failure of any country's PV system depends on the reporting of suspected ADRs and other medication safety issues. Lack of knowledge and awareness by HCPs about reporting and problems with existing reporting tools were among the frequently cited issues by key informants as constraints of the system. The spontaneous reporting system is the main means of reporting mechanisms in Ethiopia. Such kind of reporting mainly relies on the direct contributions of HCPs. In Ethiopia, reporting of ADR is fully voluntary which requires HCPs to be active participants. In a country with a low level of knowledge and awareness by HCPs regarding the importance of reporting, relying on a passive surveillance system further contributed to a low ADR reporting rate. Reports from other African countries similarly indicated very low reporting rates and the number of reports received is not sufficient to identify significant drug-related issues (Olsson *et al.*, 2010).

The qualitative exploration also indicated the presence of negligence from HCPs in reporting. A study conducted in tertiary care hospitals in Tigray Region, Ethiopia, revealed that ADRs

reporting practices among HCPs were very poor and 75% of respondents reported to have encountered one or more ADRs in their daily practice, but, only 32.1% of respondents reported ADRs (Gidey *et al.*, 2020). Another study in Amhara Region, Ethiopia, showed that a very small proportion of HCPs had encountered ADRs but were not reported to the regulatory body (Necho and Worku, 2014). Due to the low reporting by HCPs, the contribution of the NPC in reporting of ICSRs to VigiBase is very low compared to other developed countries. The cumulative number of ICSRs sent to VgiBase by the country from membership from 2008 to 2015 was 803 with 1.28 no of ICSRs per million people per year (Ampadu, 2019). A similar study conducted by Ampadu and Colleagues (2016) indicated that out of 35 SSA countries, 25 had less than 10 ICSRs per million people a year in 2015.

Concerning reporting tools, it was indicated the current manual reporting form was claimed by the respondents as not user-friendly and not suitable to report by the reporters. The paper reporting form is not fully accessible in healthcare facilities and pharmaceutical companies, it is also not suitable to fill and send back. The authority recently launched a mobile application (Med-Safety) that enables reporting of ADE. Even though this application has an advantage as an alternative platform for reporting, it has some drawbacks. The application is intended to work using android smartphones and in the presence of the internet. Also, as the system is new, it requires intensive advocacy and awareness creation. It also requires reporters to have a smartphone and a reliable internet source, and having such a facility is still a problem in developing countries like Ethiopia. Similarly, a study done in Zambia indicated the absence of the above characteristics of reporting forms (Huff-Rousselle *et al*., 2007).

The qualitative component of the present study suggested ways that enable to improvement the existing PV system that improving the effectiveness of the PV system requires working on improving the regulatory system, improving training and advocacy, provision of incentive

schemes, and increasing stakeholders' engagement among others. A qualitative study done in Nambia showed a similar finding (Adenuga *et al*., 2019).

Overall, this study indicated the positives move in RA and NPC regarding PV, however, there is still an observable gap in the overall full functionality of the PV system in healthcare facilities and pharmaceutical companies and calls the active involvement of all stakeholders including pharmaceutical companies, healthcare facilities to build an effective PV system.

# 6. Strengths and limitations of the study

The study followed a mixed study design to extract relevant information for the study theme. However, it is not without limitations.

To mention some of the strengths, this study tried to include and analyze system-based PV practices and activities of three main stakeholders who have a prominent role in maintaining and managing drug safety. The quantitative data is supplemented by qualitative findings to further explore ideas that cannot be addressed by the quantitative result including barriers for implementation of the PV system and possible solutions for further improvement. The data collection instruments (checklist and interview guide questions) were pretested in a similar setting and necessary corrections were made. Also, the use of metrics published by the WHO as PV measurement tools provides high reliability and validity for objective assessment. The findings of the study have also a potential advantage for providing a platform for future research and open the eye of other researchers on the topic and improve communication among stakeholders.

On the other hand, this study had some limitations. The study did not collect data from a representative number of health facilities (hospitals) found in the country and regulatory bodies at the regional level, which may affect the generalizability of the study results. Besides, the researcher of this study couldn't retrieve important process and outcome indicators of the PV

system due to poor recording and documentation systems of the studied organizations which may not reveal the overall picture of PV activities in the study organizations

# 7. Conclusion

In general, the study has identified PV situation to the structures, processes, and outcome levels at the NRA, pharmaceutical companies, and hospitals. The NPC under NRA has the basic PV structures, procedures, and processes in place and found at potential advantage in the implementation of PV in the country though gaps were found in the detailed management of the system. The majority of the hospitals and pharmaceutical companies lack the necessary structure, processes, and outcome PV indicators which in turn has diminished their capacity to identify, detect, prevent, ADR, and medicines' safety-related risks and protect the public.

The study also identified resource constraints and issues related to reporting as key contributing factors that impede the successful implementation of the PV system in the country. It also suggested ways to mitigate the challenges to improve the system such as system-related strategies, improving the regulatory system on PV, provision of training and awareness, encouraging stakeholders' engagement and communication, and provision of incentives for reporters.

Overall, though there is no simple means or quick fix to create a perfect PV system in the country, instead, building a robust and effective system of drug safety monitoring requires a sustained and systematic effort that requires the active involvement of all key stakeholders in the area. In this respect, creating a culture of PV is as important as having the right technical rules and regulations in place. Therefore, the finding of this study suggests that the PV system still presents some challenges that should be addressed in collaboration and involvement of key stakeholders in the sector to achieve a strong, integrated and consolidated medicine safety system in the country.

# 8. Recommendations

Based on the study findings, critical analysis of thematic contents, and the conclusions made, the following recommendations are forwarded to the respective stakeholders.

## 8.1. Recommendation for the regulatory authority

- Should work on developing consumer reporting tool to improve the reporting rate
- Should continue and work on expanding the decentralization of PV centers to different parts of the country along with the necessary inputs (infrastructure)
- Should work on inclusion of PV specific policies to adequately address PV
- Should work on ensuring the availability of reporting forms at different health facilities and pharmaceutical companies
- Should work on expanding active surveillance activities and integrate into the national PV system through collaborations with research institutions, universities, and public health programs to increase reporting and signal detection
- Should undertake a high level of discussions with various stakeholders including health facilities, pharmaceutical companies, research institutions, and academia on PV to improve collaboration and engagement
- Should work on the expansion of training, awareness creation campaign regarding PV through media or other communication channels to encourage patients to report the AEs
- Should strengthen the NPC by allocating budget, equipped with the necessary tools and equipment, put clear vision on where to reach and evaluate progress accordingly, work on knowledge transfer to build local capacity

### 8.2. Recommendation for health facilities (hospitals)

- Hospital management should work on strengthening rational use of medicines and promote structure for drug safety monitoring at their health facility level
- Health facilities need to organize PV units, strengthen drug information service unit and assign focal persons (institutional contact persons) to organize reports generated from the facilities and report to the authority.
- Should improve their documentation practices (recording and retaining) of identified, reported ADRs and other medication safety issues
- Should provide continuous training, awareness creation campaign and refresher programs on PV for HCPs
- Should work on the incorporation of PV into procedures and clinical practices in their setting

### 8.3. Recommendation for pharmaceutical companies

- Companies should organize independent PV unit/department, assign a qualified person, provide budget and other necessary inputs for the unit
- Companies should strengthen their capacity in terms of conducting PMS activities and preparing of PSURs for products under their custody
- Companies should provide continuous training to HCPs and their sales personnel /medical representatives/ regarding PV and safety reporting to increase reporting
- Companies should strengthen their activities in terms of identification, reporting, signal detection, risk-benefit evaluation, and risk management
- Companies should improve and operate the PV system with proper recording and documentation.

# 9. Suggestion for future research

The researcher recommends a similar system based study with a larger sample size that includes multi-stakeholder including health facilities out of the study area (Addis Ababa), regional regulatory bodies, public health programs, pharmaceutical importers beyond primary agents, and pharmaceutical wholesalers should be conducted to understand the overall picture of the PV system in the country.

# References


Abiri, O.T & Johnson, W.C (2019). Pharmacovigilance systems in resource-limited settings: an evaluative case study of Sierra Leone. *Journal of Pharmaceutical Policy and Practice*, 12 (1), 1-8.

Adenuga, B. A., Kibuule, D.S., Bamitale, K. D., & Rennie, T. W (2020). Effective integration of pharmacovigilance systems at public health facilities in resource-limited settings: A qualitative study. *Research in Social and Administrative Pharmacy*, 16 (8), 1111-1116.

Aljadhey, H., Mahmoud, M., Mayet, A., Alshaikh, M., Ahmed, Y., Murray, M., & Bates, D (2013). Incidence of adverse drug events in an academic hospital: a prospective cohort study. *International journal for quality in health care*, 25 (6), 648-655.

Allabi, AC & Nwokike, J (2014). A situational analysis of pharmacovigilance system in Republic of Benin. *Journal of Pharmacovigilance*.

Almandil, NB (2016). Healthcare professionals' awareness and knowledge of adverse drug reactions and pharmacovigilance. *Saudi medical journal*, 37 (12), 1359.

Almenoff, JS (2007). Innovations for the future of pharmacovigilance. *Drug safety, 30* (7), 631-633

Alomar, MJ (2014). Factors affecting the development of adverse drug reactions. *Saudi pharmaceutical journal*, 22 (2), 83-94.

Alshakka, M., Abdo Saeed, G. M., Ali, H., Prajapati, S. K., & Ibrahim, M. I (2019). Adverse Drug Reactions and Medication Errors: A Quantitative Insight in Aden, Yemen. *Journal of Young Pharmacists*, 11 (1).

Ampadu, HH (2019). Evolving national pharmacovigilance systems in Africa. Utrecht University.

Ampadu, HH, Hoekman, J, de Bruin, ML, *et al.* (2016). Adverse drug reaction reporting in Africa and a comparison of individual case safety report characteristics between Africa and the rest of the world: analyses of spontaneous reports in VigiBase®. *Drug safety*, 39 (4), 335-345

Angamo, M. T., Chalmers, L., Curtain, C. M., & Bereznicki, L. R (2016). Adverse-drug-reaction-related hospitalisations in developed and developing countries: A review of prevalence and contributing factors. *Drug safety*, 39 (9), 847-857.

Atia, A (2019). Pharmacovigilance in Libya: Current Status and Future Trends. *Indian Journal of Pharmacy Practice,* 12 (4), 267.

Barry, A, Olsson, S, Minzi, O, *et al.* (2020). Comparative Assessment of the National Pharmacovigilance Systems in East Africa: Ethiopia, Kenya, Rwanda and Tanzania. *Drug Safety*, 1-12.

Belachew, SA, Erku, DA, Mekuria, AB, *et al.* (2016). Pattern of chemotherapy-related adverse effects among adult cancer patients treated at Gondar university Referral Hospital, Ethiopia: a cross-sectional study. *Drug, healthcare and patient safety*, 8, 83.

Biswas, P (2013). Pharmacovigilance in Asia. *Journal of pharmacology & pharmacotherapeutics,* 4**,** S7.

Biswas, P & Biswas, AK (2007). Setting standards for proactive pharmacovigilance in India: The way forward. *Indian Journal of Pharmacology,* 39 (3), 124.

Bouvy, JC, De Bruin, ML & Koopmanschap, MA (2015). Epidemiology of adverse drug reactions in Europe: a review of recent observational studies. *Drug safety,* 38**,** 437-453.

Budnitz, D. S., Lovegrove, M. C., Shehab, N., & Richards, C. L. (2011). Emergency hospitalizations for adverse drug events in older Americans. *New England Journal of Medicine,* 365 (21), 2002-2012.

Caturla Goñi, M (2016). Accelerating regulatory approvals through the World Health Organization collaborative registration procedures. *Pharmaceuticals Policy and Law, 18* (1-4), 109-120.

Caudron, JM, Ford, N, Henkens, M, *et al.* (2008). Substandard medicines in resource-poor settings: a problem that can no longer be ignored. *Tropical Medicine & International Health,*13 (8), 1062-1072.

CIOMS (2001). Current challenges in pharmacovigilance: pragmatic approaches, Council for International Organizations of Medical Sciences (CIOMS).

Cockburn, R, Newton, PN, Agyarko, EK, *et al.* (2005). The global threat of counterfeit drugs: why industry and governments must communicate the dangers. *PLoS medicine,* 2**,** e100.

Coleman, J. J., & Pontefract, S. K. (2016). Adverse drug reactions. *Clinical Medicine*, *16*(5), 481.

Dal Pan, GJ (2014). Ongoing challenges in pharmacovigilance. *Drug safety,* 37**,** 1-8.

Doua, JY & Geertruyden, JPV (2014). Registering medicines for low-income countries: how suitable are the stringent review procedures of the World Health Organisation, the US Food and Drug Administration and the European Medicines Agency? *Tropical Medicine & International Health,* 19**,** 23-36.

Ethioipian Food and Drug Authorithy (2019). Food and Medicine Administration Proclamation No.1112/2019. Avilable at Food-and-Medicine-Administration-Proclamation-1112.pdf (fmhaca.gov.et). Acessed on Juanary 15, 2020

EFMHACA (2014). Guideline for Adverse Drug Events Monitoring (Pharmacovigilance). Food, Medicine and Healthcare Administration and Control Authority of Ethiopia.

Eguale, T, Tamblyn, R, Winslade, N, *et al.* (2008). Detection of adverse drug events and other treatment outcomes using an electronic prescribing system. *Drug safety,* 31**,** 1005-1016.

Elshafie, S, Roberti, AM & Zaghloul, I (2018a). Pharmacovigilance in developing countries (part II): a path forward. *International journal of clinical pharmacy,* 40**,** 764-768.

Elshafie, S, Zaghloul, I & Roberti, AM (2018b). Pharmacovigilance in developing countries (part I): importance and challenges. *International journal of clinical pharmacy,* 40**,** 758-763.

Ermias, A, Gurmesa, G, Mesfin, M, *et al.* (2011). Adverse drug reaction monitoring in Ethiopia: Analysis of case reports, 2002-2007. *Ethiopian Journal of Health Development,* 25**,** 168-173.

Eyal Zimlichman *et al*. (2018). Adverse drug event rate in Israeli hospitals: validation of an international trigger tool and an international comparison study. *The Israel Medical Association Journal (IMAJ)*.

Fornasier, G, Francescon, S, Leone, R, *et al.* (2018). An historical overview over Pharmacovigilance. *International journal of clinical pharmacy,* 40**,** 744-747.

Gautam, C, Utreja, A & Singal, G (2009). Spurious and counterfeit drugs: a growing industry in the developing world. *Postgraduate medical journal,* 85**,** 251-256.

Gidey, K, Seifu, M, Hailu, BY, *et al.* (2020). Healthcare professionals knowledge, attitude and practice of adverse drug reactions reporting in Ethiopia: a cross-sectional study. *BMJ open,* 10**,** e034553.

Gurmesa, LT & Dedefo, MG (2016). Factors affecting adverse drug reaction reporting of healthcare professionals and their knowledge, attitude, and practice towards ADR reporting in Nekemte Town, West Ethiopia. *BioMed research international*, 2016.

Gyllensten, H., Rehnberg, C., Jönsson, A. K., Petzold, M., Carlsten, A., & Sundell, K. A (2013). Cost of illness of patient-reported adverse drug events: a population-based cross-sectional survey. *British Medical Journal*, 3 (6).

Härmark, L & Van Grootheest, A (2008). Pharmacovigilance: methods, recent developments and future perspectives. *European journal of clinical pharmacology*, 64**,** 743-752.

Härmark, L & van Grootheest, K (2012). Web-based intensive monitoring: from passive to active drug surveillance. *Expert opinion on drug safety*, 11**,** 45-51.

Hsiung, P.C (2008). Teaching reflexivity in qualitative interviewing. *Teaching Sociology*, *36*(3), 211-226

Huff-Rousselle, M, Simooya, O, Kabwe, V, *et al.* (2007). Pharmacovigilance and new essential drugs in Africa: Zambia draws lessons from its own experiences and beyond. *Global public health*, 2**,** 184-203.

Hug, B. L., Keohane, C., Seger, D. L., Yoon, C., & Bates, D. W (2012). The costs of adverse drug events in community hospitals. *The joint commission journal on quality and patient safety*, *38*(3), 120-126

Hussain, R & Hassali, MA (2019). Current status and future prospects of pharmacovigilance in Pakistan. *Journal of pharmaceutical policy and practice*, 12**,** 14.

Isah, AO, Pal, SN, Olsson, S, *et al.* (2012). Specific features of medicines safety and pharmacovigilance in Africa. *Therapeutic advances in drug safety*, 3**,** 25-34.

ISCB, E (2005). Berlin declaration on pharmacovigilance. *Berlin: ISDB*.

Kabore, L, Millet, P, Fofana, S, *et al.* (2013). Pharmacovigilance systems in developing countries: an evaluative case study in Burkina Faso. *Drug safety*, 36**,** 349-358.

Kuemmerle, A, Dodoo, AN, Olsson, S, *et al.* (2011). Assessment of global reporting of adverse drug reactions for anti-malarials, including artemisinin-based combination therapy, to the WHO Programme for International Drug Monitoring. *Malaria journal*, 10**,** 57.

Kumar, V (2013).Challenges and future consideration for pharmacovigilance. *Journal of Pharmacovigilance.*

Lambert, C., Jomeen, J., & McSherry, W 2010). Reflexivity: A review of the literature in the context of midwifery research. *British Journal of Midwifery*, 18(5), 321-326.

Lindquist, AM (2003). *S*eeing and observing in international pharmacovigilance: achievements and prospects in worldwide drug safety, [Uppsala]: Uppsala Monitoring Centre.

Lindquist, M & Edwards, IR (2001). The WHO Programme for International Drug Monitoring, its database, and the technical support of the Uppsala Monitoring Center.*The Journal of rheumatology*, 28**,** 1180-1187.

Lopez-Gonzalez, E, Herdeiro, MT & Figueiras, A (2009). Determinants of under-reporting of adverse drug reactions. *Drug safety*, 32**,** 19-31.

Maigetter, K, Pollock, AM, Kadam, A, *et al.* (2015). Pharmacovigilance in India, Uganda and South Africa with reference to WHO's minimum requirements. *International journal of health policy and management*, 4**,** 295.

Mahmoud, M. A., Alswaida, Y., Alshammari, T., Khan, T. M., Alrasheedy, A., Hassali, M. A., & Aljadhey, H (2014). Community pharmacists' knowledge, behaviors and experiences about adverse drug reaction reporting in Saudi Arabia. *Saudi pharmaceutical journal*, *22*(5), 411-418.

Mammì, M, Citraro, R, Torcasio, G, *et al.* (2013). Pharmacovigilance in pharmaceutical companies: An overview. *Journal of pharmacology & pharmacotherapeutics*, 4**,** S33.

McKay, A. J., Newson, R. B., Soljak, M., Riboli, E., Car, J., & Majeed, A (2015). Are primary care factors associated with hospital episodes for adverse drug reactions? A national observational study. *BMJ open*, *5*(12), e008130.

Mekonnen, AB, Alhawassi, TM, McLachlan, AJ, *et al.* (2018). Adverse drug events and medication errors in African hospitals: a systematic review. *Drugs-real world outcomes*, 5**,** 1-24.

Mouton, JP, Njuguna, C, Kramer, N, *et al.* (2016). Adverse drug reactions causing admission to medical wards: A cross-sectional survey at 4 hospitals in South Africa. *Medicine*, 95.

Mulatu, WN & Worku, A (2014). Assessment of knowledge, attitude and practice of health professionals towards adverse drug reaction reporting and factors associated with reporting. *Journal of Pharmacovigilance.*

National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) (2015). Avilable at: http://www.nccmerp.org.

Najafi, S (2018). Importance of pharmacovigilance and the role of healthcare professionals. *Journal Pharmacovigilance*, 6 (1), 1-2.

Necho, W & Worku, A (2014). Assessment of knowledge, attitude and practice of health professionals towards adverse drug reaction reporting and factors associated with reporting. *Jouranal of Pharmacovigilance,* 2**,** 135.

Nwaiwu, O, Oyelade, O & Eze, C (2016). Evaluation of Pharmacovigilance Practice in Pharmaceutical Companies in Nigeria. *Pharmaceutical Medicine,* 30**,** 291-295.

Nwokike, J (2008). Monitoring Adverse Drug Reactions in the Public Health Programs: The Case of the Nigeria TB Program. *Submitted to the US agency for international development by the TBCAP Project*.

Nwokike, J & Eghan, K (2010). Pharmacovigilance in Ghana: A Systems Analysis. Submitted to the US agency for international development by the Strengthening Pharmaceutical Systems (SPS) program. Arlington, VA: *Management Sciences for Health.*

Nwokike, J & Joshi, M (2009). Assessment of Pharmacovigilance and Medicine Safety System in Rwanda. US Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program, Arlington, VA: *Management Sciences for Health*.

Nwokike, J, Ludemann, E & Thumm, M (2013). Comparative Analysis of Pharmacovigilance Systems in Five Asian Countries. Submitted to the US Agency for International Development by the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program., *Arlington, VA : Management Sciences for Health.*.

Olowofela, A (2018). Evaluation of pharmacovigilance system performance in South-South Nigeria.

Olsson, S, Pal, SN & Dodoo, A (2015). Pharmacovigilance in resource-limited countries. *Expert review of clinical pharmacology,* 8**,** 449-460.

Olsson, S, Pal, SN, Stergachis, A, *et al.* (2010). Pharmacovigilance activities in 55 low-and middle-income countries. *Drug safety,* 33**,** 689-703.

Opadeyi, AO, Fourrier-Réglat, A & Isah, AO (2018).Assessment of the state of pharmacovigilance in the South-South zone of Nigeria using WHO pharmacovigilance indicators.*BMC Pharmacology and Toxicology,* 19**,** 27.

Palaian, S 2018. Pharmacovigilance Practices and Activities: Issues, Challenges, and Future Direction. *Social and Administrative Aspects of Pharmacy in Low-and Middle-Income Countries.* Elsevier.

Palappallil, D. S., Ramnath, S. N., & Gangadhar, R (2017). Adverse drug reactions: Two years' experience from a tertiary teaching hospital in Kerala. *National Journal of Physiology, Pharmacy and Pharmacology,* 7 (4), 403

Pal SN, Dodoo A, Mantel A, Olsson S (2011).The world medicines situation. Geneva: WHO

Pirmohamed, M, Atuah, KN, Dodoo, AN, *et al.* (2007). Pharmacovigilance in developing countries. *BMJ: British Medical Journal,* 335**,** 462.

Pote, S., Tiwari, P., & D'cruz, S (2007). Medication prescribing errors in a public teaching hospital in India: A prospective study. *Pharmacy Practice (Internet), 5*(1), 17-20.

Rolfes, L., van Hunsel, F., Taxis, K., & van Puijenbroek, E. (2016). The impact of experiencing adverse drug reactions on the patient's quality of life: a retrospective cross-sectional study in the Netherlands. *Drug safety*, 39 (8), 769-776.

Rottenkolber, D., Hasford, J., & Stausberg, J. (2012). Costs of adverse drug events in German hospitals-a microcosting study. *Value in health*, 15 (6), 868-8

Santoro, A, Genov, G, Spooner, A, *et al.* (2017). Promoting and protecting public health: how the European Union pharmacovigilance system works. *Drug safety,* 40**,** 855-869.

Shanko, H & Abdela, J (2018). Knowledge, attitudes, and practices of health care professionals toward adverse drug reaction reporting in Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia: a cross-sectional study. *Hospital pharmacy,* 53**,** 177-187.

Stausberg, J (2014). International prevalence of adverse drug events in hospitals: an analysis of routine data from England, Germany, and the USA. *BMC health services research*, 14 (1), 1-9.

Swain, S., & Patra, C. N (2014). Impact of Pharmacovigilance in Healthcare System: Regulatory Perspective. *Pharmaceut Reg Affairs, 3 (5),* e143.

Strengthening Pharmaceutical Systems (2009). Supporting pharmacovigilance in developing countries: The systems perspective. Submitted to the US Agency for International Development by the SPS Program. Management Sciences for Health Arlington.

Strengthening Pharmaceutical Systems Program (2011). Safety of Medicines in Sub-Saharan Africa: Assessment of Pharmacovigilance Systems and their Performance. Management Sciences for Health Arlington, VA.

Strengthing Pharmaceutical Systems (2009). Indicator-based pharmacovigilance assessment tool: A manual for conducting assessments in developing countries

Suleman, F (2010). Pharmacovigilance-who is responsible and why should we care? *SA Pharmaceutical Journal*, 77**,** 56-58.

Talbot, J & Nilsson, B (1998). Pharmacovigilance in the pharmaceutical industry. *British journal of clinical pharmacology*, 45**,** 427-431.

Uppsala Monitoring Center (2013). Avilable at http://www.who-umc.org.

Van Grootheest, K (2003). The dawn of pharmacovigilance. *International journal of pharmaceutical medicine*, 17**,** 195-200.

Vargesson, N (2015). Thalidomide-induced teratogenesis: History and mechanisms. *Birth Defects Research Part C: Embryo Today: Reviews*, 105**,** 140-156.

Venulet, J & Helling-Borda, M (2010). WHO's international drug monitoring--the formative years, 1968-1975: preparatory, pilot and early operational phases. *Drug safety*, 33**,** e1-e1.

Walter, S. R., Day, R. O., Gallego, B., & Westbrook, J. I (2017). The impact of serious adverse drug reactions: a population-based study of a decade of hospital admissions in New South Wales, Australia. *British journal of clinical pharmacology*, 83(2), 416-426.

WHO (2001). Current Challenges in Pharmacovigilance: Pragmatic Approaches, Report of CIOMS Working Group V. *Geneva: WHO*.

WHO (2002a). The importance of pharmacovigilance.

WHO (2002b). Safety of medicines: a guide to detecting and reporting adverse drug reactions: why health professionals need to take action.

WHO (2004). Pharmacovigilance: ensuring the safe use of medicines.

WHO (2006). The safety of medicines in public health programmes: pharmacovigilance, an essential tool.

WHO (2010). Minimum requirements for a functional pharmacovigilance system. *Geneva: WHO*.

WHO (2015). WHO pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems. *WHO pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems.*

WHO (2016). Improving the quality of medical products for universal access. [Online]. [15 July 2020]. Available from: https://www.who.int/medicines/regulation/fact-figures-qual-med/en/

WHO (2013). Glossary of terms used in Pharmacovigilance. *WHO Programme for International Drug Monitoring*.

Wilbur, K (2013). Pharmacovigilance in the middle east. *Drug safety,* 36**,** 25-30.

National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) (2015). http://www.nccmerp.org.

Uppsala Monitoring Center (2013). Available at http://www.who-umc.org.

WHO (2015). WHO Pharmacovigilance Indicators. WHO; Geneva

Zhou L & Rupa AP. (2017). Categorization and association analysis of risk factors for adverse drug events. Eur J Clin Pharmacol, 74 (4): 389-404.

# ANNEXES

***Annex I*: In-Depth Interview**

## Addis Ababa University

## College of Health Sciences

## School of Pharmacy

### Department of Pharmaceutics and Social Pharmacy

### Participants' information sheet and consent form for an in-depth interview

My name is____. I'm a postgraduate (MSc) student at Addis Ababa University, College of Health Sciences, School of Pharmacy, Department of Pharmaceutics, and Social Pharmacy. As part of this degree in Regulatory Affairs, I am conducting a research entitled **"Pharmacovigilance System in Ethiopia: Implementation Status and Challenges**". The research could mainly serve for the country to identify modifiable factors in relation to medicine safety and plan intervention accordingly. If you agree to take part in this study you will be among those who will contribute towards strengthening the PV system in the country. Your information and others participating in the study will collectively use by policymakers in strengthening the system.

To obtain the necessary information, I am delivering an interview. The in-depth interview is prepared to assess the current PV system in the country. The interview will take 25-45 minutes of your time and the interview will be held at your convenient location and time. Your participation is purely voluntary and the information you provide will be kept completely confidential. Direct quotes might be taken from your response to be used in written and verbal reports of the paper but your name will never be written and aggregate responses from different respondents will only be identified only by codes. However, voice recorded (tape recorder) may be used during the interview. Your honest response to the question is of paramount importance for the successful completion of the study. There is no right or wrong answer and you can have clarification for any doubt regarding the questions.

Are you willing to respond to the questions? Yes/No

# Interview Guide Questions

**Instruction:** the following general interview guide questions are intended to collect in-depth information from key informants regarding the current PV system in Ethiopia.

1. Code no: _____
2. Name of the Interviewer: _____
3. Date of interview: _____
4. Place of interview:_____

***Part 1: Key informants' Profile***

1. Gender A. Male B. Female
2. Age :_____(in years)
3. Profession: _____
4. Academic qualification: _____
5. Position: _____
6. Work experience:_____(in years)

**Part *2: General Interview guide Questions***

1. How do you describe the present PV system/working procedure/ in Ethiopia? **Probe on**: the legal framework (available policies, laws, regulations, guidelines…), government commitment, human resources or infrastructure, budget, reporting system, feedback and communication among stakeholders)
2. How do you describe the support of the top management on the implementation of PV system in your institution? **Probe on**: Provision of training for health professionals, allocation of budget, organizational policy on medicine safety...)
3. In your opinion, what would be the negative consequences of not having a proper PV system in your institution and country as a whole?
4. In your opinion, what are the possible factors/challenges/ that contribute as barriers to the PV system not working in a way as it should be? **Probe on**: law and regulations, funding issue, trained human resource, stakeholders' coordination, and communication, medicine policy…
5. In your opinion, do you think that there is a need to change the system about medicine safety in the country? If yes, what benefit would it have?

6. In your opinion what could be the role of each respective stakeholder (regulatory authority (EFDA), Pharmaceutical companies, and health facilities) to efficiently and effectively improve the PV system in the country?
7. What could be your possible suggestions to improve the current PV system in the country?
8. Would you like to provide any additional comments about the PV system in Ethiopia?

***Thank you very much for your cooperation!***

***Annex II*:** Amharic Version of the Interview Guide

# አዲስ አበባ ዩኒቨርሲቲ

# ጤና ሳይንስ ኮሌጅ

# የፋርማሲ ት/ቤት

## የፋርማሲዉቲክስና ሶሻል ፋርማሲ ትምህርት ክፍል

### የቃለ መጠይቅ ፎርም

**መግቢያ**

እኔ ____ በአዲስ አበባ ዩኒቨርስቲ ጤና ሳይንስ ኮሌጅ ፋርማሲ ት/ቤት በፋርማሲዉቲክስና ሶሻል ፋርማሲ ትምህርት ክፍል በድህረ ምረቃ ፕሮግራም የሁለተኛ ዲግሪ (ማስተርስ) ተማሪ ስሆን የመመረቂያ ፅሁፌን በኢትዮጵያ ዉስጥ ስላለው የመድሀኒት ደህንነት ክትትል ስርአት (ፋርማኮቪጂላንስ ሲስተም) ላይ እየሰራሁ እገኛለሁ። የዚህ ጥናት ዋና አላማ ከመድሃኒት ደህንነት ጋር በተያያዘ ሊቀረፉ የሚችሉ ችግሮችን ለይቶ በማውጣት በሀገሪቱ ውስጥ የተሻለ የመድሀኒት ደህንነት ክትትል ስርአት እንዱጎለብት ለማድረግ ነው። ስለሆነም ይህንን አርዕስት በተመለከተ መረጃ ለመሰብሰብ ይጠቅም ዘንድ ከታች የሚገኘውን ቃለመጠይቅና ቼክሊስት አዘጋጅቻለው።

በዚህ ጥናት በመሳተፍዎ በእርስዎ ጤና፣ አካልና ስነልቦና ላይ የሚደርስ ምንም አይነት ጉዳት አይኖርም። የእርስዎ ተሳትፎ ግን በሀገሪቱ ለሚተገበረው ትክክለኛ የመድሀኒት ደህንነት ክትትል ስርአት መሻሻል ይረዳል። ጥናቱ ሙሉ በሙሉ በፈቃደኝነት ላይ የተመሰረተ ሲሆን ከእርስዎ የሚገኘው መረጃ በሚስጢር የሚያዝ ይሆናል። መረጃ በሚሰበሰብበትም ጊዜ የእርስዎን ስምም ሆነ እርስዎን ሊያመለክቱ የሚችሉ ነገሮች አይካተቱም። በጥናቱ የመሳተፍ ወይም ያለመሳተፍ የእርስዎ ምርጫ ሲሆን በጥናቱ መሃል (ቃለ ምጠይቅ ጊዜ) አቋርጠው የመውጣት መብትዎም የተጠበቀ ነው። ለቃለ መጠይቁ የሚሰጧቸው ምላሾች ሁሉ በሚስጥር የተጠበቁ ሲሆኑ ከጥናት አድራጊው ውጪ ማንም ሰው የሰጡትን መረጃ ሊያገኘው አይችልም።መረጃ ሙሉ በሙሉ ለመመዝገብ ይቻል ዘንድ በቃል-መጠይቁ ጊዜ የድምፅ መቅጃ መሳሪያ መጠቀም ያስፈልጋል።

ይህንን ፅሁፍ በተመለከተ ትክክል ወይም የተሳሳተ የሚባል መልስ የሌለ ሲሆን ነገር ግን የእርስዎ ሀቀኛ የሆነ መልስ ለፅሁፌ እውነተኛነት እና በስኬት መጠናቀቅ ትልቅ ሚና ስላለው እንዲተባበሩኝ በትህትና እጠይቃለው። ቃለ መጠይቁ ከ25-45 ደቂቃ የሚፈጅ ሲሆን በመረጡት ቦታና ግዜ ሊካሄድ ይችላል። በመቀጠልም እርስዎ ፈቃደኛ ከሆኑ መጀመር እንችላለን።

**አዎ/አይደለም**

## ቃለ መጠይቅ ለሚደርግላቸው የተዘጋጀ ቃለ መጠይቅ ፎርም

**መመሪያ:** ይህ የቃለ መጠይቅ አጋዥ ጥያቄዎች (Interview Guide Questions) በኢትዮጵያ ዉስጥ ስላለው የመድሃኒት ደህንነት ክትትል ስርዓት (ፋርማኮቪጂላንስ ሲስትም) በሚመለከት ከመድሃኒት ኩባንያዎች ማለትም ከሀገር ዉስጥ መድሃኒት አምራቾችና አስመጪዎችና አለም አቀፍ የመድሃኒት አምራች ኩባንያዎች፤ ከጤና ተቋማት (ሆስፒታሎች) እና ከኢትዮጵያ ምግብና መድሃኒት ባለስልጣን መረጃ ለመሰብሰብ የተዘጋጀ አጠቃላይ መጠይቅ ነው።

1. መለያ ኮድ: _____
2. ቃለ መጠይቁ ያደረገው ስም: _____
3. የቃለ መጠይቁ ቀን: _____
4. ቃለ መጠይቁ የተደረገበት ቦታ: _____

### *ክፍል 1: የቃለ መጠይቅ ተሳታፊው አጠቃላይ መግለጫዎች*

1. ፆታ፡ ሀ. ወንድ ለ. ሴት
2. እዴሜ: _____(በአመት)
3. የሙያ መስክ:_____
4. የትምህርት ደረጃ:_____
5. አሁን ያሉበት የስራ መደብ: _____
6. የስራ ልምድ (በአመት): _____

### *ክፍል 2: ጥናቱን የተመለከቱ ጥያቄዎች*

1. በአሁኑ ጊዜ በሀገራችን ያለው የመድሃኒት ደህንነት ክትትል ስርዓት (ፋርማኮቪጂላንስ ሲስተም) እንዴት ይገልጹታል? (ከህግ ማዕቀፍ ፤ የመንግስት ቁርጠኝነት፥ የባለድሽ አካላት ትብብርና መረጃ መለዋወጥ፥ የሰለጠነ የሰው ሃይል መኖር ፥ በጀት ወዘተ…)
2. ያሉበት ተቋም/ድርጅት/ የመድኃኒት ደህንነት ክትትል ስርዓት እንዲዘረጋ ከተቋሙ ከፍተኛ ኃላፊዎች ያለው ተነሳሽነትና ድጋፍ እንዴት ይገልጹታ? (ከተቋሙ የመድሃኒት ደህንነት ፖሊሲ ፣የባለሙያ ስልጠና፣ የገንዘብ ድጋፍ ወዘተ…)
3. ትክክለኛ የመድሃኒት ደህንነት ክትትል ስርአት አለመኖር በጤናው ዘርፍ የሚያስከትለው አሉታዊ ተጽዕኖ (ጉዳት) እንዴት ይገልጹታል?
4. በእርስዎ አስተያየት በአሁኑ ጊዜ በሀገራችን ያለው የመድሃኒት ደህንነት ክትትል ስርዓት በአግባቡ አለመኖር ዋና ተግዳሮቶች (ምክንያቶች) ምንድናቸው ብለው ያስባሉ?

5. በእርስዎ እይታ አሁን ያለዉን የመድሃኒት ደህንነት ክትትል ስርአት መቀየር አለበት ብለው ያስባሉ? መቀየሩ በጤናው ዘርፍ ምን ጠቀሜታ ይኖረዋል?
6. በእርስዎ እይታ አሁን ያለዉን የመድሃኒት ደህንነት ክትትል ስርአት እንዲሻሻልና እንዲተገበር ምን አይነት እርምጃ መወሰድ አለበት ብለው ያስባሉ?
7. አሁን በሀገራችን ያለው የመድሃኒት ደህንነት ክትትል ስርዓት እንዲሻሻል ከእያንዳንዱ ባለድርሻ አካላት (stakeholders) ማለትም ከኢትዮጵያ ምግብና መድኃኒት ባለስልጣን (EFDA) ፤ ከጤና ተቋማት (Health facilities) ፤ ከመድኃኒት ተቋማት (ከሀገር ዉስጥ መድሀኒት አምራቾች፥ አስመጪዎችና አከፋፋዮች ወዘተ…) ምን ይጠበቃል ብለው ያስባሉ?
8. በመጨረሻም በአሁኑ ጊዜ በሀገራችን ስላለው የመድኃኒት ደህንነት ክትትል ስርዓት በሚመለከት የሚያስተላለፉት ተጨማሪ መልእክት ወይም አስተያየት ካለ?

***ስለ ትብብርዎ ከልብ አመሰግናለሁ።።***

***Annex III:*** Pharmacovigilance system assessment checklist (For Hospitals and Pharmaceutical Companies)

## Addis Ababa University

## College of Health Sciences

## School of Pharmacy

### Pharmacovigilance System in Ethiopia: Implementation Status and Challenges

**Instruction**: the following checklist is adapted from WHO PV system assessment tool (2015) and intended to assess the PV system of pharmaceutical companies in the country (local medicine manufacturers and importers, Multinationals) and hospitals in Addis Ababa.

Please, put a tick mark (√) on **'Yes'** and **'No'** column and write a specific number that shows process and outcome indicators on the given space.

1. Code: _____
2. Name of data collector: _____
3. Date of data collection: _____
4. Type of the institution /Company (general hospital, specialized hospital, local manufacturer, importer, multinational manufacturer): _____
5. **Ownership type** (government, private): _____

| S/N | Assessment Questions | Overall Answer | | |
|---|---|---|---|---|
| | **Core Structural Indicators** | **Yes** | **No** | **Remark** |
| 1 | Does the company/institution/have a regulatory unit? | | | |
| 2 | Does the company/institution/have a PV unit? | | | |
| 3 | Is the PV unit standalone from the regulatory unit? | | | |
| 4 | Does the PV unit have human resources to carry out its functions properly? | | | |
| 6 | Does the company have a qualified person for PV (QPPV)? | | | |
| 7 | Is there any regular financial provision (statutory budget) for the PV unit? | | | |
| 8 | Is there written SOPs present for PV activities? | | | |
| 9 | Are PV SOPs present signed by relevant persons, documented, and officially adopted? | | | |
| 10 | Is there a tool for PV information dissemination (newsletter, information bulletin/ website)? | | | |
| 10 | Does the company/institution/has a safety systems (database) support? | | | |

| | | | | |
|---|---|---|---|---|
| 11 | Is there a standard ADR reporting form in the setting? | | | |
| 12 | Is there a process in place for collection, recording and analysis of ADR reports? | | | |
| | **Complementary Structural Indicators** | | | |
| 1 | Is there a dedicated computer for PV activities? | | | |
| 2 | Are there functioning and accessible communication facilities in the PV unit? | | | |
| 3 | Is there library or any other reference source for drug safety information? | | | |
| 4 | Is there a computerized case report management system? | | | |
| 5 | Does the PV unit organize training courses? | | | |
| | 5a: for health professionals? | | | |
| | 5b: for the general public? | | | |
| 5 | Is there a source for data on consumption and prescription of medicines? | | | |
| 6 | Is there a programme (including a laboratory) for monitoring the quality of pharmaceutical products? | | | |
| 7 | Does the company /Institution/have an SOP for the following: | | | |
| | a. Processing ICSRs | | | |
| | b. Periodic PSUR | | | |
| | c. Risk-management plans | | | |
| 8 | Are the staffs trained on risk-management plans? | | | |
| | | | | |
| 9 | Does the company have marketed products with a risk-management plan? | | | |
| 10 | Does the /institution/company have reports that have been processed and sent to: | | | |
| | a. Parent company? | | | |
| | b. Regulatory Authority? | | | |
| 11 | Were the processed reports sent within the stipulated company/health authority/ timelines? | | | |
| 12 | Are safety signals and significant safety issues immediately communicated to health workers, regulatory authority and the public? | | | |
| | **Core process indicators** | | | |
| 1 | Total number of ADR reports received last calendar year | | | |
| 2 | Current total no of reports in the company's/institution's/database | | | |
| 3 | Percentage of total annual reports acknowledged/issued/feedback | | | |
| 4 | Percentage of total reports subjected to causality assessment in the past year | | | |

| | | | | |
|---|---|---|---|---|
| 5 | Percentage of total annual reports satisfactorily completed and submitted to the national PV Centre in the previous year | | | |
| 6 | Percentage of reports of therapeutic ineffectiveness in the previous year | | | |
| 7 | Percentage of reports on medication errors reported in the previous year? | | | |
| 8 | No of active surveillance activities are or were initiated, ongoing or completed in the past 5 years? | | | |
| **Complementary process indicators** | | | | |
| 1 | Percentage of total reports sent in the previous year by the different stakeholders | | | |
| | 1a: percentage of the total reports sent by medical doctors | | | |
| | 2b: percentage of the total reports sent by dentists | | | |
| | P2c: percentage of the total reports sent by pharmacists | | | |
| | P2d: percentage of the total reports sent by nurses or midwives | | | |
| 2 | No face to face training sessions were conducted on PV in the previous year | | | |
| 3 | No individuals received face to face training in pharmacovigilance in the previous year | | | |
| | 3a. number of health professionals | | | |
| | 3b: number of individuals from general public | | | |
| **Core Outcome/impact/ indicators** | | | | |
| 1 | No of signals detected by PV unit in the last 5 years | | | |
| 2 | Percentage of preventable ADRs reported in the previous year out of the total number of ADRs reported | | | |
| 3 | Percentage of prescription forms prescribing medicines with potential for interaction | | | |
| 4 | No of medicine-related hospital admissions per 1000 admissions | | | |
| 5 | No of medicine-related deaths per 1000 persons served by the hospital per year | | | |
| 6 | Average cost (US$) of treatment of medicine-related illness | | | |
| 7 | Average duration of medicine-related extension of hospital stay? | | | |
| 9 | Average cost (US$) of medicine-related hospitalization? | | | |
| 10 | No of active surveillance activities initiated, ongoing or completed the last 5 years | | | |
| 11 | No of “Dear health care professional” letters or any other type of safety alert letters developed and distributed in the last year | | | |
| **Complementary outcome indicators** | | | | |

| | | | | |
|---|---|---|---|---|
| 1 | Percentage of preventable ADRs out of the total no of ADR reported in the preceding year? | | | |
| 2 | Medicine-related congenital malformations per 100 000 births in the setting | | | |
| 3 | Percentage of prescriptions with medicines exceeding recommended dose | | | |
| 4 | Percentage of prescriptions containing medicines with potential for interaction | | | |
| 5 | Percentage of patients receiving information on the use of their medicines and on potential ADRs associated with those medicines | | | |

***Annex IV:*** Pharmacovigilance System Assessment Checklist (For Regulatory Authority)

## Addis Ababa University

## College of Health Sciences

## School of Pharmacy

## Department of Pharmaceutics and Social Pharmacy

### Pharmacovigilance System in Ethiopia: Implementation Status and Challenges

**Instruction:** The following PV assessment checklist is adapted from the WHO PV assessment tool (2015) and intended to collect data from the NRA (EFDA).

| S/N | Assessment Questions | Overall Answer | | |
|---|---|---|---|---|
| | **Core Structural Indicators** | **Yes** | **No** | **Remark** |
| 1 | Is there a statutory provision (national policy, legislation) for PV? | | | |
| 2 | Is there a national ADRs database that exists? | | | |
| 3 | Is the ADR database computerized? | | | |
| 4 | Is there a PV Centre or unit with standard accommodation? | | | |
| 5 | Is there any regular financial provision (statutory budget) for the PV Centre? | | | |
| 6 | Does the PV Centre have human resources to carry out its functions properly? | | | |
| 7 | Are ADR reports sent to the WHO database in Uppsala? | | | |
| 8 | Does the PV center publish an ADR bulletin/Newsletter/? | | | |
| 9 | Is there a clear communication strategy for routine communication and crisis communication? | | | |
| 10 | Is there a standard ADR reporting form in the setting? | | | |
| | 10a: Are there relevant fields in the standard ADR form to report suspected medication errors? | | | |
| | 10b: Are there relevant fields in the standard ADR form to report suspected counterfeit/ substandard medicines? | | | |
| | 10c: Are there relevant fields in the standard ADR form to report therapeutic ineffectiveness? | | | |
| | 10d: Are there relevant fields in the standard ADR form to report suspected misuse, abuse, and/or dependence on medicines? | | | |
| | 10e: Is there a standard ADR reporting form for the general public | | | |

| | | | | |
|---|---|---|---|---|
| 11 | Is there a process in place for collection, recording and analysis of ADR reports? | | | |
| 12 | Is there a tool for PV information dissemination (newsletter, information bulletin or website)? | | | |
| 13 | Is there a national ADR or PV advisory committee or an expert committee in the setting capable of providing advice on medicine safety? | | | |
| **Complementary Structural Indicators** | | | | |
| 1 | Is there a dedicated computer for PV activities? | | | |
| 2 | Are there functioning and accessible communication facilities in the PV Centre? | | | |
| 3 | Is there a library or other reference source for drug safety information? | | | |
| 4 | Is there a computerized case-report management system? | | | |
| 5 | Is there a program (including a laboratory) for monitoring the quality of pharmaceutical products? | | | |
| 6 | Is there an essential medicines list that is in use? | | | |
| 7 | Are PV data considered when developing the main standard treatment guidelines? | | | |
| 8 | Does the PV Centre organize training courses for health professionals & the general public? | | | |
| 9 | Are web-based PV training tools available *for* health professionals & the general public? | | | |
| 10 | Are there requirements mandating MAHs to PSURs? | | | |
| 11 | Was there any regulatory decision based on local PV data in the last 2 years? | | | |
| 12 | Is there a mechanism for provision of feedback to reporters? | | | |
| **Core Process Indicators** | | | | |
| 1 | Total no of ADR reports received in the previous calendar year | | | |
| | 1a: Total no of ADR reports received in the previous year per 100,000 people in the population | | | |
| 2 | No of reports (current total no) in the national/local/database | | | |
| 3 | Percentage of total annual reports acknowledged/issued feedback/ to reporters | | | |
| 4 | Percentage of total reports subjected to causality assessment in the past year | | | |
| 5 | Percentage of total annual reports satisfactorily completed and submitted to the national PV Centre in the previous year | | | |
| | 5a: Of the reports satisfactorily completed and submitted to the national PV Centre, what percentages were communicated to the WHO database? | | | |
| 6 | Percentage of reports of therapeutic ineffectiveness received in the previous year | | | |

| | | | | |
|---|---|---|---|---|
| 7 | Percentage of reports on medication errors reported in the previous year | | | |
| 8 | Percentages of registered pharmaceutical companies that have a functional PV system | | | |
| 9 | No of active surveillance activities are or were initiated, ongoing or completed in the past 5 years | | | |
| | **Complementary process indicators** | | | |
| 1 | Percentage of HFs that had functional PV unit (i.e. submits ≥ 10 reports annually to the PV Centre)? | | | |
| 2 | Total no of reports received per million populations per year | | | |
| 3 | No of face to face training session's conducted on PV in the previous year<br>a. No of face to face PV training sessions for health professionals<br>b. No of face to face PV training sessions for the general public | | | |
| 4 | No of registered products with a PV plan or risk management strategies from MAH exist in the country<br>A. Percentage of registered products with a PV plan and/or a risk management strategy from MAHs in the country | | | |
| 5 | Percentage of MAHs submitting periodic safety update reports (PSURs) to the regulatory authority as stipulated in the country | | | |
| | **Core Outcome/Impact Indicators** | | | |
| 1 | Total no of signals generated in the past 5 years by the PV Centre | | | |
| 2 | No of regulatory actions taken in the preceding year consequent on national PV activities | | | |
| | 2a: product label changes (variation) | | | |
| | 2b: safety warnings on medicines to:<br>2bi. Health professionals<br>2bii. The general public | | | |
| | 2c: Withdrawals of medicines | | | |
| | 2d: No of other restrictions on the use of medicines | | | |
| 3 | Percentage of preventable ADRs out of the total number of ADRs reported in the preceding year | | | |
| 4 | Percentage of medicines that are counterfeit/substandard/ in the pharmaceutical market | | | |
| 5 | Number of analysis report published in the last two years | | | |
| 6 | No of reports that have been submitted to Uppsala monitoring Centre in the last two years | | | |
| 7 | No of products voluntarily withdrawn by MAHs because of safety concerns in last year? | | | |

***Annex V*:** Ethical Clearance


በ ፋርማሲ ት/ቤት

የኢቲካል ሪቪው ቦርድ

**አዲስ አበባ ዩኒቨርሲቲ**
**Addis Ababa University**

**School of Pharmacy**

**Ethical Review Board**


ቀን Date: April 08, 2019

ቁጥር Ref. No.: ERB/SOP/67/04/2019

To: **Sisay Endale**
School of Pharmacy

**Re:** **Ethical Clearance**

It is to be recalled that you submitted a study proposal entitled ***"Assessment of pharmacovigilance system in Ethiopia"*** for ethical approval by the School's Ethical Review Board (ERB). The Board thoroughly reviewed the proposal based on its operational guidelines and found it to fulfill all ethical requirements stipulated in the guidelines. This is, therefore, to inform you that the proposal is ethically approved for implementation.

With best regards,

Arebu Issa
Chairperson, ERB


☎ 00251156 02 12 ✉ 1176 ቴሌክስ Telex: 21205 ፋክስ Fax: 00251(11)1558566 ቴሌግራም Cable: AAUNIV