MINISTRY OF HEALTH& HUMAN SERVICE
FEDERAL REPUBLIC OF SOMALIA

Somali Pharmacovigilance Guideline

Interim National Medicines Regulatory Authority (NMRA)

November, 2023

First edition

Executive Summary

Amongst its many functions as specified in the National Medicine Policy endorsed in 2014, the Ministry of Health, specifically the National Medicine Regulatory Authority (NMRA) is responsible for regulating and controlling the pharmaceutical service and ensuring the continuous availability and accessibility of safe and effective medicines to all segments of the population.

The Interim NMRA has developed this guideline for healthcare professionals and the public on detecting, reporting and monitoring adverse drug reactions and substandard medicinal products.

The purpose of this guideline is to support healthcare professionals to participate in the continuous surveillance of the safety and efficacy of medicinal products and vaccines, which are used in clinical practice for public and private health facilities. Its ultimate goal is to enhance efforts in ensuring that safe, efficacious, and quality medicines are made available for Somali people.

This guideline states the issues on what to report, why to report when to report, where to report, and how to report. In consultation with various stakeholders, the NMRA will review these guidelines and tools periodically to ensure that they continue to meet the goals of the Pharmacovigilance system in the country.

The reporting requirements defined in this guideline are based mainly on the guidelines of the International Conference for Harmonization (ICH), the United States Food and Drug Administration (FDA), and the World Health Organization (WHO).In addition; pieces of information are also adapted from:

- UMC. Safety Monitoring of Medicinal Products. Guidelines for setting up and running a Pharmacovigilance Centre. Uppsala, the Uppsala Monitoring Centre, 2000.
- EMA. European Medicines Agency Pharmacovigilance system manual. Version 1.3. Amsterdam, EMA, 2013 (updated in 2021).
- ANSM. Bonnes Pratiques de Pharmacovigilance. Paris, Agence Nationale de Securité des Médicaments et Produits Sanitaires, 2022.
- WHO. Covid-19 vaccines: safety surveillance manual. Geneva, WHO, 2020.
- CIOMS. Cumulative Pharmacovigilance Glossary: Version 1.0. Geneva, CIOMS, 2021.

All healthcare professionals, public health programs, and public and private suppliers are encouraged to report all suspected adverse drug reactions to the pharmacy service section to help safeguard the patient's health.

Acknowledgment

We would like to express our sincere gratitude and appreciation to all those who contributed to the preparation of the National Pharmacovigilance Guideline of Somalia. The collaborative effort and invaluable support from various stakeholders have been instrumental in the successful development of this crucial document. We would like to acknowledge the following individuals and organizations:

First and foremost, we extend our heartfelt thanks to the African CDC (Centers for Disease Control and Prevention) and MasterCard, and the AKROSE RESEARCH for their unwavering financial and technical support throughout the entire process. Their financial support and commitment to strengthening pharmacovigilance systems in Africa have been invaluable in shaping the guidelines.

We would like to extend our deepest appreciation to Dr. Albert, the consultant who was hired to draft the National Pharmacovigilance Guidelines. Albert's dedication, expertise, and meticulous attention to detail have played a pivotal role in crafting a comprehensive and robust framework.

We would also like to acknowledge the Interim National Medicines Regulatory Authority (NMRA) role, especially the Pharmacovigilance unit for their valuable consultation throughout the development of this guideline. Their insights and recommendations have greatly enriched the content and ensured its alignment with the national regulatory framework.

Furthermore, we express our sincere thanks to the representatives from the Federal and State Ministries of Health, Public Health Programs, Health professionals, Pharmaceutical private sectors and WHO including Dr. Abdinasir Moalim Ibrahim, Dr. Mohamed Abdirahman Omar (Qalbi), Dr. Yusuf Omar Mohamed, Dr. Hodan Ahmed Ali, Dr. Farhan Bashir Hassan, Dr. Hassan Elmi, Mukhtar Abdi Shube, Ahmed Abdikadir Khalif (Zakaria), Hodan Yusuf Hassan, Abdi Karim Ali Omar, Mustaf Moalim Mohamed, Dr. Farhiyo Abdinur, Dr. Libaan Hassan Mohamud, Dr.Yahye Ahmed Nageye, Dr. Abdifitah Farah Aden, Khadar Hussein Mohamud, Raho Mohamed Ali, Hussein Sheikh Ahmed, Abdirahman Mohamed Mohamud, Abbas Ahmed Adam, Dr. Ahmed Adam Mohamed, Dr. Farah Mohamed Sharawe, Dr. Shafi Abdullahi Moalim, Dr abdirahim Nageye, Dr. Hamza, Dr.Abdullahi Ali Ameriko, Saynab Abdulle Mohamud, Abdiwali Mohamud Ali, Dr.Mohamed Amin Adawe, Ahmed Abdullahi Abdi, Kheyrad Abdulle Abdirahman, Haji Shucayb Abdilahi, Mohamud Garun Gas, Issack Bashir Abdi, Mustafa Mohamed Aden, and Dr. Abdinur Hussein Ahmed, who involved in the consultation process and their active participation, valuable input, and commitment to ensuring the safety and efficacy of medical products in Somalia have been invaluable.

We are indebted to each and every individual and organization mentioned above for their dedication, expertise, and unwavering commitment to safeguarding the health and well-being of the Somali population. Without their contributions, the development of the National Pharmacovigilance Guideline of Somalia would not have been possible.

Thank you once again for your invaluable support and collaboration

Forward Message

I would like to express my deepest appreciation to all those who have contributed to the development of the first-ever Pharmacovigilance (PV) Guidelines for Somalia. This milestone achievement would not have been possible without your valuable input and dedication.

I am particularly grateful for the financial and technical support provided by the African CDC, MasterCard, and Akros Research, which has played a vital role in the development of these guidelines. Your contribution has been instrumental in ensuring that our healthcare system can effectively monitor and address the safety of medical products.

Now, it is imperative that we focus on the implementation of this Pharmacovigilance guideline. I strongly urge the interim National Medicine Regulatory Authority, Public Health Programs, Health facilities, Health professionals, Patients, and Private pharmaceutical importers to fully adopt and adhere to the guidelines. This will guarantee the safety of medical products and promote public health in Somalia.

Let us recognize the significance of this guideline in improving our health system and monitoring the safety of medical products. By diligently following this guideline, we can enhance our healthcare infrastructure and safeguard the well-being of our citizens.

Thank you for your unwavering commitment to advancing healthcare in Somalia. Together, we can achieve a brighter and healthier future for all.

H.E Dr. Ali Haji Adam Abubakar

Minister of Health and Human Services
Federal Government of Somalia

ACRONYMS AND ABBREVIATIONS

ADR Adverse drug reaction

AEFI Adverse events following the immunization

PV Pharmacovigilance

SPVS Somalia Pharmacovigilance System

WHO World Health Organization

NMRA National Medicine Regulatory Authority

MAH Market Authorization holder

HFs Health Facilities

PHPs Public Health Programs

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SECTION 1: INTRODUCTION

1.1 Background

Amongst its many functions as specified in the National Medicine Policy endorsed in 2014, the Ministry of Health, specifically the National Medicine Regulatory Authority (NMRA) is responsible for regulating and controlling the pharmaceutical service and ensuring the continuous availability and accessibility of safe and effective medicines to all segments of the population.

Medicines and vaccines are essential for individual patients and public health. They have the ability to cure or prevent certain conditions, but, on the other hand, they can also produce unwantedor harmful effects, known as adverse drug reactions (ADRs) and adverse effects following immunization (AEFIs).
The beneficial effects of medicines and vaccines are measured by their "efficacy", while "safety" or "risk" refers to the magnitude and characteristics of ADRs/AEFI. Ideally, any treatment should have high efficacy and low risk for the individual that receives it.

Medicinal products have undergone preclinical and clinical studies (clinical trials) to ensure their efficacy, quality, and basic safety profile before market authorization is granted. However, clinical trials are small studies conducted on a sample population so, they can't provide information on rare ADRs or AEFIs, or those appearing in a specific population due to environmental or genetic particularities. For this reason, any new medicine or vaccine requires careful post-marketing surveillance to detect all previously unknown ADRs quickly.

Besides medicinal products, using herbal medicines also entails certain risks, despite being considered "natural" and "safe". Nonetheless, several herbal medicines are quite active, and their use may be associated with adverse effects and interactions with medicinal products. Furthermore, they scape quality control. So, continuing vigilance is needed. Additionally, substandard and counterfeit drugs are on the market, and can also produce harmful outcomes, beyond the therapeutic failure. Instances of calamities claiming the lives of numerous children due to using a toxic solvent have been documented. So, continuous surveillance must be kept in place to detect such products.

Pharmacovigilance is an essential aspect of patient care that aims to identify new information about potential hazards, prevent harm to patients, and ensure the best outcome of treatment with medications and other products. This science allows for the identification, assessment, and understanding of risks, including risk factors when medicines are used after marketing authorization. It also enables measures to be taken to prevent adverse reactions to patients.

There are two major approaches used in pharmacovigilance: spontaneous or passive reporting and active surveillance systems. Information from spontaneous adverse drug reactions reporting, post-authorization studies, clinical trials, case-control studies, and other post-market studies include information on adverse effects that is used to aid decision-making. The information from these sources may lead to changes in product labels, restrictions on product use, strengthening of specific warnings, or product withdrawal.

This Guideline has been developed to provide requirements, procedures, roles, responsibilities, and activities in pharmacovigilance for public health programs, the Ministry of Health, Marketing Authorization Holders, Academia, research institutions, interim National Medicine Regulatory Authority (INMRA), health facilities, healthcare providers, patients/consumers, and regional and international stakeholders. This guideline outlines the reporting requirements for the different stakeholders, data management, communication, training requirements, monitoring, and evaluation of pharmacovigilance systems.

Similarly, various tools for data collection, including reporting forms, have also been appended to the guidelines for easy reference. The implementation of these guidelines will facilitate reliance and mutual recognition of regulatory actions and assurance of the quality and safety of medical products and other health technologies produced, imported, exported, or traded in Somalia.

The reporting requirements defined in this guideline are based mainly on the guidelines of the International Conference for Harmonization (ICH), the United States Food and Drug Administration (FDA), and the World Health Organization (WHO). In addition, pieces of information are also adapted from:

- *UMC. Safety Monitoring of Medicinal Products. Guidelines for setting up and running a Pharmacovigilance Centre. Uppsala, the Uppsala Monitoring Centre, 2000.*
- *EMA. European Medicines Agency Pharmacovigilance system manual. Version 1.3. Amsterdam, EMA, 2013 (updated in 2021).*
- *ANSM. Bonnes Pratiques de Pharmacovigilance. Paris, Agence Nationale de Securité des Médicaments et Produits Sanitaires, 2022.*
- *WHO. Covid-19 vaccines: safety surveillance manual. Geneva, WHO, 2020.*
- *CIOMS. Cumulative Pharmacovigilance Glossary: Version 1.0. Geneva, CIOMS, 2021.*

All healthcare professionals, public health programs, and public and private suppliers are encouraged to report all suspected adverse drug reactions to the Interim National Medicine Regulatory Authority to help safeguard the patient's health.

The Interim NMRA along with the Ministry of Health shall be responsible for enforcing this guideline in Somalia and also contribute to the regional, continental, and international harmonization initiatives for effective product quality and safety monitoring.

1.2 Legal Framework of Pharmacovigilance

The existing legal framework for pharmacovigilance is established through the National Medicine Policy, which was endorsed in 2014. Subsequent ministerial decrees were issued in 2016, 2020, and 2023 to further enforce the policy and ensure the safety of medical products in the country. Additionally, the Medicine Bill currently being discussed in parliament instructs the authorities to develop pharmacovigilance guidelines and implement them effectively.

1.3 Scope

The Somalia PV guideline provides information on various activities that help ensure safety when it comes to medicines, biologics, medical devices, herbal medicines, and medicated cosmetics. These activities include conducting, assessing, monitoring, and reporting, all of which are crucial for ensuring the safety of these products.

This document will describe (i) the roles and detailed operational procedures of the SPVS and (ii) the practical aspects of how to identify adverse drug reactions (ADRs) and adverse events following the immunization (AEFIs) during daily clinical care, and how to report them to the SPVS.

1.4 Classification of ADRs

There are many ways of classifying ADRs. For example, ADRs can be classified according to their seriousness (mild, serious, fatal). ADRs can also be classified depending on the organ/system they affect (skin, digestive tract, cardiovascular system, psychiatric reactions, etc.). But a common and useful way to classify ADRs is according to their mechanism. For example, Rawlins and Thomson provided the following classification:

Type A (*augmented*):

- Dose-dependent and predictable. Type A ADRs are explained because of the medicine's mechanism of action. Usually, they are exaggerated pharmacological effects.
- Fairly common, dose-related (i.e. more frequent or severe with higher doses) and may often be avoided by using doses appropriate (or adjusted) to the individual patient.
- Examples include bradycardia with β-adrenoceptor antagonists, hemorrhage with anticoagulants, or drowsiness with benzodiazepine anxiolytics.

Type B (*bizarre*):

- Also denominated idiosyncratic ADRs. These are dose-independent and unpredictable; they have an allergic or hypersensitivity background. Characteristically, Type B ADRs occur in only a minority of patients and display little or no dose relationship.
- Although their incidence and morbidity are low, their mortality may be high.
- The most common example is an allergic reaction after administering penicillin to an allergic patient. Other cases include malignant hyperthermia of anesthesia, acute porphyria, and many immunological reactions.

Besides the original A and B classification, other authors have suggested additional types of ADRs:

Type C (*chronic*):

- Type C includes chronic reactions related to long-term use of the suspected medicine and the amount of medicine (dose).
- Some examples are nephropathy after years of exposure to analgesics, tardive dyskinesia or parkinsonism after using certain neuroleptics.

Type D (*delayed*):

- Delayed but dose-independent effects.
- Some examples include carcinogenicity (e.g., by immunosuppressants) or teratogenicity (such as the fetal hydantoin syndrome).

Type E (*end of use*):

- ADRs that appear just after finishing a prolonged treatment.

- Examplesareacute adrenal insufficiency due to abrupt steroid cessation or rebound effects after abrupt cessation of benzodiazepines.

Type F(*failure*):

- This is a new category, which is interesting because it helps to identify cases of therapeutic failure due to several causes, such as substandard products, antimicrobial resistance or using an inappropriate dosage for the patient.

SECTION 2: PHARMACOVIGILANCE SYSTEMS

2.1 Objectives

The SPVS has the following objectives:

1. To improve patient care and safety concerning medicines, vaccines, and all other medical and paramedical interventions.
2. To facilitate the early detection of problems related to the use of medicines, vaccines or medical devices, and communicate the findings promptly, with special emphasis on previously unknown ADRs or AEFIs, unusual clusters of ADRs, and problems related to low-quality, substandard or substandard or falsified products.
3. To contribute to assessing the benefit, effectiveness, and risk of medicines, encouraging their safe, rational, and more effective (including cost-effective) use.
4. To promote understanding, education, and clinical training in Pharmacovigilance and its effective communication to health professionals, manufacturers, and the public.
5. To create an ADR database for the Somali population.

Secondarily, the SPVS will contribute to the following:

- Foster the reporting culture and, consequently, improve the prescription, dispensing and use of medicines.
- Increase the population's trust in new medicines and vaccines because the SPhVS monitors any unknown or unexpected adverse reaction.

2.2 SPVS – Stakeholders Involved

These objectives can be attained thanks to the engagement of different stakeholders with well-defined roles that will be described in another section. Grouped by general functions, these stakeholders are:

a) Governance and structure support

- Ministry of Health
- Healthcare professionals
- Health facilities
- Public health programs
- Donors
- NGOs

b) Providing reports

- Healthcare professionals (GPs and physicians, pharmacists, nurses, community agents, etc.)
- Citizens (patients or representatives of the patient such as a family member or a community leader).
- Private Health Facilities
- Market Authorization Holders (MAH)

c) Communication and training support

- Academia and research institutions
- Professional Associations
- Media (TV, radio, and social media)

d) International PhV Support

- WHO Collaborating Center for International Drug Monitoring (Uppsala Monitoring Centre, WHO-PIDM).
- Africa CDC
- National PV System in other countries

2.3 Pharmacovigilance Structure-Governance

The Somalia Pharmacovigilance System comprises:

1) National Pharmacovigilance section under the interim NMRA.
2) State Pharmacovigilance Focal Points
3) National PV committee.

2.4 Minimal Requirements to Establish PV System in Somalia

Pharmacovigilance processes require proper facilities and equipment to be effective. This includes office space, IT systems, storage space (computer, internet), and Access to publications.
These facilities should be designed and maintained to meet quality objectives for pharmacovigilance. It is very critical to have at least one Pharmacist and one Medical Doctor with the required training in pharmacovigilance knowledge used for their intended purpose at the federal and state level.

2.5 Quality Systems

The quality system encompasses the structure, procedures, processes, responsibilities, and resources of the organization. It plays a vital role in monitoring, evaluating, and managing the process, ensuring compliance with international quality standards, and maintaining records.

All stakeholders involved in pharmacovigilance activities need to establish a quality system to attain desired outcomes and meet quality objectives.

2.6 Training of The Pharmacovigilance Personals

The Ministry of Health, Interim NMRA, and all other institutions involved in pharmacovigilance activities must ensure that they possess a sufficient number of personnel who are skilled, knowledgeable, and adequately trained to perform pharmacovigilance tasks. Moreover, the institution should establish an inclusive training package for pharmacovigilance.

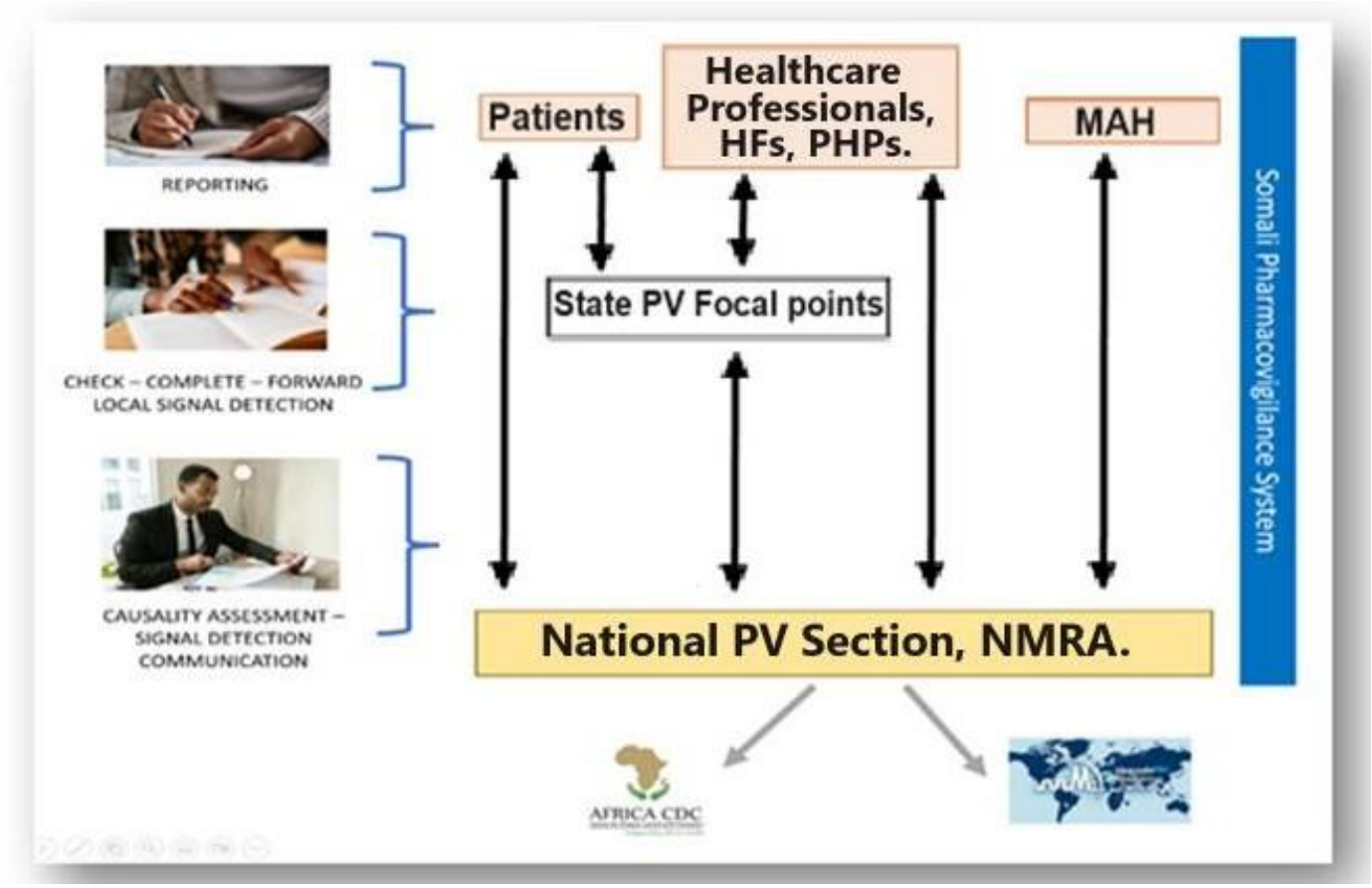
2.7 Communications Among Pharmacovigilance Stakeholders

The Somali Pharmacovigilance System (SPVS) is located in the interim NMRA of the Federal Ministry of Health and Human Services of the Somali Government.
It is based on reporting adverse events by healthcare professionals, citizens, and manufacturers.
The SPVS follows a modified model of the World Health Organization Program for International Drug Monitoring (WHO-PIDM), a long-established, cost-effective, and useful method for detecting signals by identifying previously unknown ADRs to medicinal products or changes in the patterns of known ADRs that aims at ensuring that patients obtain safe and efficacious medicinal products.

The SPVS is based on a decentralized reporting system for healthcare professionals and citizens, and centralized reporting for manufacturers. Suspected case reports of ADR are sent, respectively, to the State Pharmacovigilance focal points or the National Pharmacovigilance section via well-defined reporting tool (portal system in the Website, Email, and Phone).
Reporting of AEs by healthcare professionals and citizens is optional but highly encouraged because the success of a PV system and its impact on patient safety and public health depends on a high reporting rate.
However, reporting is mandatory for pharmaceutical manufacturers or product registrants to monitor their products in the market and report any suspected undesirable effects to the Interim NMRA.
Furthermore, public health programs, including Malaria, Human Immune Deficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS), Tuberculosis (TB), NTD, and vaccines, should introduce ADR/AEFI reporting in their programs. This includes providing awareness to the health workers during seminars and training to report adverse drug reactions. So, a close collaboration between the Interim NMRA in the Ministry of Health and Public Health programs is necessary.

The Figure shows the structure of the SPVS, the role of the different professionals involved in the reporting system, the flow of the reports and the international links of the SPVS.
In summary, the Somali National Pharmacovigilance unit (Coordinating unit) is located in the Interim NMRA of the Federal Ministry of Health and Human services. The SPVS – CC receives the reports validated and complete from the Federal Member States Centers (FMS – PVC) and also receives the reports sent by the manufacturers. The CC is also responsible for national communication concerning safety issues and international liaison with Africa CDC and other regional organisms, as well as the WHO-PIDM in Uppsala.

Figure 1: Flow of information



SECTION 3: PHARMACOVIGILANCE PROCESSES, ROLES & RESPONSIBILITIES

3.1 PHARMACOVIGILANCE PROCESSES

The Interim NMRA shall establish a pharmacovigilance system for the collection and evaluation of information relevant to the risk-benefit balance of medical products. The INMRA shall continuously monitor the safety profile of the products marketed in Somalia and take appropriate action where necessary, and monitor the compliance of MAHs with their obligations with respect to pharmacovigilance.

3.2 ROLES AND RESPONSIBILITIES OF THE STAKEHOLDERS:

3.2.1 The National Pharmacovigilance Section:

- This section is under the Interim NMRA of the Federal Ministry of Health and Human Services FGS and it acts as of coordinating Centre for pharmacovigilance activities in the country and is also the country reference for WHO and other international stakeholders. The Head of the National Pharmacovigilance Section (National Pharmacovigilance Focal Point) is responsible for the following:
  - Coordinating pharmacovigilance activities nationwide;
  - Creating awareness of pharmacovigilance among health professionals, healthcare providers, marketing authorization holders, and the public;
  - Post-marketing surveillance of high-risk pharmaceutical products;
  - Establishing and maintaining a functional national database on ADRs and other medicine-related problems to identify unknown or poorly specified adverse effects;
  - Led national and international collaboration on safety issues.
  - Contributing to the fight against counterfeit medicines.
  -

3.2.2 The Federal State Members' Pharmacovigilance Focal Points

Every state will nominate a PV Focal point with relevant qualifications (Medical doctor or pharmacist) and his/her role and responsibilities are:

1. receiving all the reports originating in the state;
2. ensuring the integrity and completeness of the reports;
3. contacting the reporters to obtain lacking information;
4. act as a contact person for the National Pharmacovigilance section of the Interim NMRA;
5. regularly meet with the National PV committee and act as a natural member of this *committee*
6. stay alert on possible signals originating locally;
7. Be the receptor of PV information produced by the SPVS and disseminate the relevant information among the reporters of the State.

3.2.3 The National Pharmacovigilance Committee (NPVC)

The advisory committee works under the interim NMRA of the Federal Ministry of Health. The NPVC oversees and evaluates potential safety and quality issues arising from using medical products in Somalia. The NPVC will also recommend possible regulatory measures based on Pharmacovigilance data received from various sources. The NPVC will comprise eleven experts from different disciplines, including a Head of National Pharmacovigilance, State Pharmacovigilance focal points, General physician, internal medicine, clinical pharmacologists, epidemiologist, and toxicologists. The Head of the National Pharmacovigilance section in the NMRA of the Federal Ministry of Health will chair this committee.

3.2.4 Public Health Programs

Public Health Programs (PHP) such as HIV/AIDS, TB, and Malaria, Expanded Programs on Immunization, Maternal, and Child Health programs, CDs etc.) Shall be actively engaged in pharmacovigilance activities with the following roles and responsibilities:

1. To add a budget for pharmacovigilance activities in their strategic plan,
2. Develop a pharmacovigilance plan for medical products used by the programs
3. Should have a focal person (pharmacist or medical doctor), to coordinate PV activities in collaboration with the Interim National Pharmacovigilance Section of the Interim National Medicine Regulatory Authority,
4. Distribute reporting forms (ADRs/AEFI, Patient Alert Cards, suspected poor quality reporting, medical device adverse event reporting forms, etc.) in Program sites,
5. Collect data using appropriate reporting forms,
6. Collaborate with the Interim NMRA/PV Section on active surveillance of their products,
7. Develop risk management plans and follow-up patients,
8. Train healthcare providers in reporting adverse drug events/AEFI including other aspects of pharmacovigilance,
9. Promote rational and safe use of medical products by healthcare providers,
10. Educate and inform patients on the importance of reporting adverse drug events/AEFIs,
11. Assess and communicate the risks and effectiveness of medicinal products used in the specific PHP in collaboration with the Interim NMRA/PV Section,
12. Develop protocols and conduct active surveillance of medical products used in the program
13. Monitor and evaluate the impact of pharmacovigilance interventions.
14. Put in place a mechanism to disseminate Safety information to health professionals and the general public,
15. Implement feedback/regulatory action taken for safety reasons on medical products,

3.2.5 Health Facilities

Public and private health facilities shall have the following roles and responsibilities in Pharmacovigilance:

1) Allocate budget for pharmacovigilance activities,
2) Receive and distribute ADR/AEFI reporting forms to health care providers,
3) Sensitize healthcare providers on Pharmacovigilance activities

4) Detect, investigate, manage and report ADRs/AEFI and take appropriate action to prevent ADRs and AEFIs,
5) Communicate appropriate safety information to healthcare providers and the community including patients,
6) Identify a focal person to coordinate pharmacovigilance activities within the health facility.
7) Maintain a register of suspected ADRs including medication errors.
8) Public and private hospitals shall establish functional Medicine and Therapeutic Committees (MTCs) with role and responsibilities.

3.2.5 Marketing Authorization Holders, Manufacturers, Local Technical Representatives

The MAH/Manufacturers shall ensure that there are appropriate pharmacovigilance and risk management systems in place to assure responsibility for their products on the market. Representatives from the National Pharmacovigilance Committee operate pharmacovigilance activities under the supervision of QPPV of the MAH/Manufacturer shall Continuously monitor pharmacovigilance data, the examination of options for risk minimization and prevention and that appropriate measures are taken by the marketing authorization holder,

3.2.6 Academia

Academia shall have the following roles and responsibilities:

- Develop and incorporate the Pharmacovigilance training modules in the curricula of health professionals,
- Provide pre-service, in-service, and continuous professional development training on Pharmacovigilance,
- Participate actively in the development of PV training materials,
- Carry out safety studies related to medical products,
- Collaborate with the Interim National Medicine Regulatory Authority, MAH, and other relevant stakeholders in PV activities,
- Sharing of safety information and study findings related to medical products and health technologies with the Authority.

3.2.7 Research Institutions

Research institutions shall have the following roles and responsibilities:

- Carry out safety studies related to medical products and health technologies,
- Collaborate with Authority, MAH, and other relevant stakeholders in PV activities,
- Sharing of safety information and study findings related to medical products and health technologies with the Authority.

3.2.8 Development Partners

Development partners in collaboration with the Ministry of Health and other stakeholders shall provide both financial and technical support during the implementation of pharmacovigilance activities at all levels.

3.2.9 Ministry of Health and Human Services, FGS

The Ministry of Health shall;

- Develop and review policies and legal frameworks to strengthen pharmacovigilance activities
- ensure effective integration of pharmacovigilance activities within public health programs and health facilities,
- Mobilize and provide resources for pharmacovigilance activities to health facilities and NMRA.

3.2.10 Patients, Health care Providers, and Consumers

Patients, health care providers, and consumers should report any suspected adverse reaction or event associated with the use of medical products and health technologies immediately to the nearest health facility, health care provider, MAH or directly to the NMRA.

3.2.11 Collaboration with Uppsala Monitoring Centre (UMC)

The Interim NMRA shall collaborate with the WHO Collaborating Centre for Safety Monitoring, African CDC, and other regional harmonization.

SECTION 4: ADVERSE EVENTS REPORTING

4.1 Who should report AEs?

Everyone is encouraged to report adverse events through the reporting structure. Reporters from both the public and private health sectors are expected to submit reports to the Authority. These shall include medical doctors, dentists, pharmacists, clinical officers, pharmaceutical technologists, nurses, public health programs, staff in medical laboratories, community health workers, pharmaceutical manufacturing companies, marketing authorization holders (MAHs), importers, distributors, Patients or patient representatives/ guardians, researchers and principal investigators.

4.2 What should be reported?

- All serious and fatal ADRs/AEFI
- Lack of Efficacy
- Overdose
- Any other Observations

The Somali PV System (SPVS) has an official reporting form that allows the standardization of the reports and facilitates the collection of as much relevant information as possible to conduct a good causality analysis.

4.3 Minimum Criteria for Reporting

It is recommended that as much information as possible be collected at the time of the initial report. However, for the purpose of regulatory reporting, the minimum data elements for an ADR case are:

- an identifiable reporter
- an identifiable patient,
- an adverse reaction (including at least date of onset), and a
- suspect medical product (including, at least, starting date).

The lack of any of these four elements means that the case is considered incomplete.

4.4 When to report?

Any suspected AE/AEFI should be reported as soon as possible to the relevant PV focal points and communicated to the Interim NMRA of the Ministry of Health and Human Service via telephone, online reporting system, e-mail, or in writing according to the following timelines:

4.4.1 Healthcare Professionals and/or Patients:

- Fatal and other serious adverse events/adverse drug reactions should be notified within 24 hours and a complete report shall be submitted by Healthcare Professional within seven (7) calendar days,
- Non-serious adverse events/adverse drug reactions shall be reported within seven (7) calendar days

4.4.2 Marketing Authorization Holders:

- Fatal and other serious adverse events/adverse drug reactions that have occurred in Somalia shall be notified to the Interim National Medicine Regulatory Authority as soon as possible but not later than seven (7) calendar days;
- In case all the information needed is not available within 7 days, a complete report for fatal and other serious adverse events/adverse drug reactions that have occurred in Somalia shall be reported within fifteen (15) calendar days.
- Local non-serious adverse events/adverse drug reactions reports shall be submitted within 30 calendar days;
- All foreign serious and non-serious adverse events/reactions to medical products registered/marketed in Somalia shall be reported as per regular timelines within the Periodic Safety Update Report (PSUR)/ Periodic Benefit/Risk Evaluation Report (PBRER).

4.4.3 Timelines for providing feedback

The timelines for providing feedback are the following:

- The NMRA/ PV Section shall acknowledge receipt of safety reports as soon as possible but not later than 7 days and also shall provide feedback within 30 calendar days

4.5 How and where to report?

All the filled AE/AEFIA reporting forms shall be sent to the NMRA/ PV Section either electronically or via email at pv@nmra.gov.so

4.6 Confidentiality of ADR Reports

Any information related to the reporter and patient must be kept strictly confidential.

4.7 Active Surveillance Reporting

Active surveillance, in contrast to passive surveillance, seeks to ascertain completely the number of adverse events via a continuous pre-organized process. An example of active surveillance is the follow-up of patients treated with a particular drug through a risk management program.

4.8 Vigilance of The Medical Products

The Interim NMRA recognizes that various PHPs will have reporting requirements that do not fit well with the aforementioned requirements.

4.8.1 Adverse Events Following Immunization (AEFI)

Vaccine safety monitoring is a collaborative process that involves the National Vaccines and Immunization Programs, NMRA, healthcare providers, consumers, partners, and other stakeholders. The AEFIs shall be reported using the available reporting form.
AEFIs are grouped into five categories which include;

- vaccine product-related reactions.
- vaccine quality defect-related reactions
- immunization error-related reactions.
- immunization anxiety-related reaction, and
- coincidental event

4.8.1.1 What AEFIs to report?

Healthcare providers and caregivers should report any AEFI that is of concern. Both minor and serious AEFI cases should be reported.
This includes:

- Serious AEFIs: adverse events or reactions that result in death, hospitalization, persistent or significant disability or incapacity (e.g. paralysis), or are potentially life-threatening
- Signals and events associated with a newly introduced vaccine
- AEFIs caused by immunization error
- Allergic reaction e.g. anaphylaxis, hives, bronchospasm, edema
- Seizures
- Any events causing significant parental/caregiver or community concern
- Swelling, redness, soreness at the site of injection if it lasts more than 3 days or swelling extends beyond the nearest joint, inability to move the limb.

4.8.1.2 Conducting an AEFI investigation

Additional investigation on some AEFIs may be required to determine the underlying cause of the AEFI. The purpose of the investigation is to:

- Confirm the reported diagnosis and timing of AEFI
- identify details of vaccine(s) administered
- determine the cause of AEFI
- document the outcome of the reported adverse event
- determine whether the reported event is a single incident or part of a cluster
- identify and address the operational aspects of the immunization program which may have led to immunization errors

4.9 Adverse events following the Use of medical devices

An event/incident including a malfunction or deterioration in the characteristics or performance due to a medical device is subject to be reported if it meets the following criteria:
For IVDs (In-vitro diagnostics) where there is a risk that an erroneous result would either

4.10 Adverse Events Due to Traditional/ Herbal Medicines

Adverse events (AEs), Case reports of acute and chronic poisoning (toxicity), and adverse interactions with other medical products and food related to herbal products shall be reported to the Interim National Medicines Regulatory Authority.

4.11 Reporting of Suspected Poor Quality Medical Products

All healthcare providers in the private and public sectors can alert The Interim NMRA of the Federal Ministry of Health and Human Services on product quality issues. The poor-quality issues may include color change, separation of components, powdering, crumbling, caking, molding, change of odor, mislabeling, incomplete pack, suspected contamination, questionable stability, defective components, poor packaging/poor labeling, therapeutic failures and receiving expired medicines.

SECTION 5: RISK MANAGEMENT SYSTEMS

The aim of a risk management plan (RMP) is to document the risk management system considered necessary to identify, characterize and minimize medical products and health technologies' important risks.
The medical products RMP shall contain:

- the identification or characterization of the safety profile of the medical products.
- the planning of pharmacovigilance activities to characterize and quantify clinically relevant risks, and to identify new adverse reactions/events (the 'pharmacovigilance plan');
- The planning and implementation of risk minimization measures, including the evaluation of the effectiveness of these activities.

5.1 Risk Minimizations Measures

Risk minimization measures are interventions intended to:

- Prevent or reduce the occurrence of adverse reactions associated with the exposure to a medical product, and reduce their severity or impact on the patient should adverse reactions occur.
- Plan and implement risk minimization measures and assessing their effectiveness are key elements of risk management. Safety concerns of a medicinal product are normally adequately addressed by routine risk minimization measures in the risk management plan.
- Facilitate informed decision-making to support risk minimization when prescribing, dispensing and/or using a medicinal product.

5.2 Causality Assessment & Signal Management

The collected adverse events should be systematically assessed to determine whether they are possibly related to the studied (or supplied) medical products. The Interim NMRA shall adopt to use the WHO Causality Assessment methods and/or the Naranjo algorithm. For vaccines, causality assessment shall follow the WHO User Manual for causality assessment of AEFI.

5.3 Signal Management

Signals can arise from a wide variety of data sources. Common sources for signals include spontaneous reporting systems, active surveillance systems, studies, and scientific literature reports. The process of signal management involves the following: Signal detection, Signal evaluation and validation, Signal prioritization, and Signal communication.

5.3.1 **Signal Detection:** Signal detection refers to the systematic process of identifying potential new safety concerns or signals from available data sources, such as spontaneous reports, clinical trials, literature, and other sources. It involves the identification of statistically significant and clinically relevant patterns, associations, or unusual

occurrences that may indicate a previously unrecognized adverse event associated with a specific medicine.

5.3.2 **Signal Evaluation and Validation:** Signal evaluation and validation involve a comprehensive analysis and assessment of the identified signals to determine their clinical relevance and validity. It includes a detailed review of the available data, such as case reports, epidemiological studies, or experimental data, to establish a causal relationship between the medicine and the adverse event. This evaluation helps determine whether further investigation or action is needed.

5.3.3 **Signal Prioritization**: Signal prioritization involves assigning a level of priority to the identified signals based on their potential clinical significance and public health impact. The prioritization process considers factors such as the severity of the adverse event, the number of reported cases, the plausibility of the association, and the likelihood of detecting similar signals in other data sources. Prioritization helps allocate resources effectively for further investigation or risk management activities.

5.3.4 **Signal Communication:** Signal communication involves the dissemination of information related to the identified signals to relevant stakeholders, including regulatory authorities, healthcare professionals, and the public. It aims to ensure the timely and appropriate sharing of safety information, enabling informed decision-making regarding the use of medical products. Communication may occur through regulatory updates, safety advisories, public announcements, or educational materials.

SECTION 6: SAFETY COMMUNICATION

6.1 Aims of Safety Communication

The aims of safety communication are:

- Providing timely, evidence-based information on the safe and effective use of medical products.
- Facilitating changes to healthcare practices (including self-medication practices) where necessary;
- Changing attitudes, decisions, and behaviors in relation to the use of medical products.
- Supporting risk minimization behavior;
- Facilitating informed decisions on the rational use of medical products and health technologies.

6.2 Steps in Safety Communication

The risk communication process involves the following:

- Identifying the issue and its context
- Assessing the risk and benefits
- Identifying and analyzing options
- Selecting a strategy
- Implementing the strategy
- Monitoring and evaluation of results

6.3 Target Audience

The primary target audiences for safety communication issued by NMRA and marketing authorization holders should be patients, healthcare providers, consumers, and healthcare professionals who prescribe, handle, dispense, administer, or take medical products.

6.4 Content of Safety Communication

Safety communication shall contain the following:

- Important new information on any authorized medical product which has an impact on the medicine's risk-benefit balance under any conditions of use;
- The reason for initiating safety communication is clearly explained to the target audience;
- Any recommendations to healthcare professionals and patients on how to deal with a safety concern;
- Information on any proposed change to the product information (e.g. the summary of product characteristics (SmPC) or Package Information Leaflet (PIL));
- A reminder of the need to report suspected adverse reactions in accordance with national spontaneous reporting systems.

6.5 Communication Channels

Different communication channels are existed and shall include the following:

- Direct Healthcare Professional Communication (DHPC)
- Communication materials from the interim NMRA targeted at healthcare professionals
- Press communication
- Website
- Social media and other online communications
- Bulletins and newsletters
- Responding to enquiries from the public
- Other means such as publications, scientific and professional journals
- Conferences, seminars and workshops

6.6 Effectiveness of Safety Communications

Safety communication is considered effective when the message transmitted is received and understood by the target audience in the way it was intended, and appropriate action is taken by the target audience.

SECTION 7: REGULATORY ACTIONS

7.1 Reliance and Mutual Recognition

Regulatory decisions, reports, and activities related to the vigilance of medical products shall also base on a reliance approach as detailed in the related guidelines.

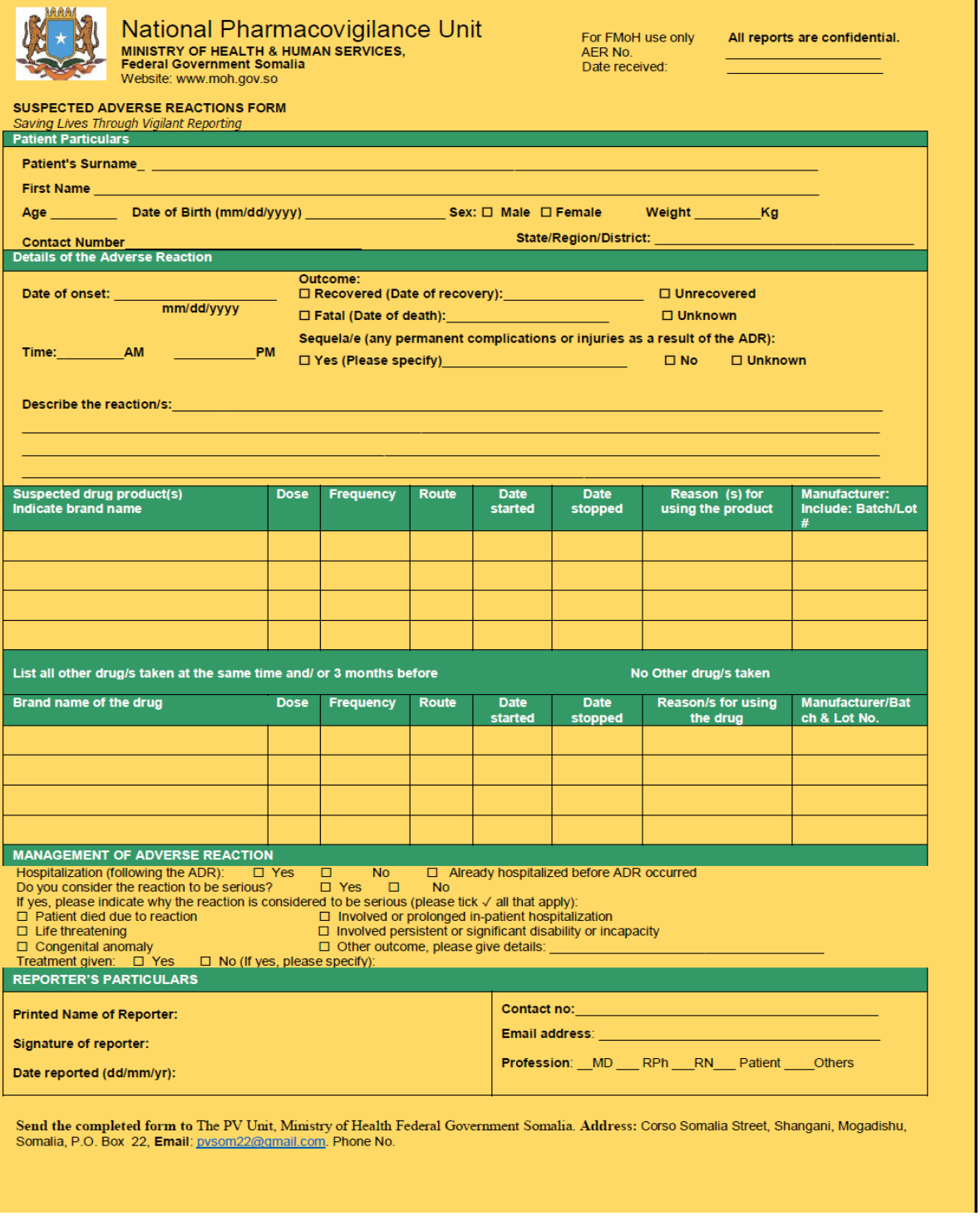
7.2 Withdrawal of A Product from The Market on Risk-Benefit Grounds

After the risk-benefit evaluation of a product, the risks outweigh the benefits, and the proposed risk minimization measures are considered inadequate to redress the balance, the medical product should be withdrawn from the market and Healthcare Professionals and Patients/the public should be informed as appropriate. In case the MAH withdraws the medical product due to safety concerns, they shall be obliged to immediately report to NMRA.

7.4 Appeal

For products that have been suspended and/or canceled marketing authorization by the interim NMRA, MAH may make a written appeal to the Interim NMRA to review its decision. All notice of appeals must be made within thirty (30) calendar days from the date of the NMRA's notification. MAH shall make an appeal by giving grounds for review for each reason given for the rejection of his/her product.
The grounds for the request shall be based on the information that was submitted in the product's dossier. Any additional or new information that was not earlier submitted will not be accepted. The Authority may review or uphold its earlier decision

Annex I: Adverse Drug Reaction reporting form



National Pharmacovigilance Unit
MINISTRY OF HEALTH & HUMAN SERVICES,
Federal Government Somalia
Website: www.moh.gov.so

For FMoH use only
AER No.
Date received:

All reports are confidential.

SUSPECTED ADVERSE REACTIONS FORM
Saving Lives Through Vigilant Reporting

Patient Particulars

Patient's Surname_ _____

First Name _____

Age _____ Date of Birth (mm/dd/yyyy) _____ Sex: ☐ Male ☐ Female Weight _____Kg

Contact Number _____ State/Region/District: _____

Details of the Adverse Reaction

Date of onset: _____ mm/dd/yyyy

Time:_____AM _____PM

Outcome:
☐ Recovered (Date of recovery):_____ ☐ Unrecovered
☐ Fatal (Date of death):_____ ☐ Unknown

Sequela/e (any permanent complications or injuries as a result of the ADR):
☐ Yes (Please specify)_____ ☐ No ☐ Unknown

Describe the reaction/s:_____

Suspected drug product(s) Indicate brand name	Dose	Frequency	Route	Date started	Date stopped	Reason (s) for using the product	Manufacturer: Include: Batch/Lot #

List all other drug/s taken at the same time and/ or 3 months before — No Other drug/s taken

Brand name of the drug	Dose	Frequency	Route	Date started	Date stopped	Reason/s for using the drug	Manufacturer/Batch & Lot No.

MANAGEMENT OF ADVERSE REACTION

Hospitalization (following the ADR): ☐ Yes ☐ No ☐ Already hospitalized before ADR occurred
Do you consider the reaction to be serious? ☐ Yes ☐ No
If yes, please indicate why the reaction is considered to be serious (please tick ✓ all that apply):
☐ Patient died due to reaction ☐ Involved or prolonged in-patient hospitalization
☐ Life threatening ☐ Involved persistent or significant disability or incapacity
☐ Congenital anomaly ☐ Other outcome, please give details: _____
Treatment given: ☐ Yes ☐ No (If yes, please specify):

REPORTER'S PARTICULARS

Printed Name of Reporter:

Signature of reporter:

Date reported (dd/mm/yr):

Contact no:_____

Email address: _____

Profession: __MD ___ RPh ___RN___ Patient ____Others

Send the completed form to The PV Unit, Ministry of Health Federal Government Somalia. Address: Corso Somalia Street, Shangani, Mogadishu, Somalia, P.O. Box 22, Email: pvsom22@gmail.com. Phone No.

Annex II: Immunization register

IMMUNISATION (EPI) REGISTER (R-06) **Month** **Year**

Serial Number	Date of First Visit (DD/MM/YY)	Birth Date (DD/MM/YY) / Age	Child Card Number	Child Full Name	Mother / Guardian Name / Mobile Number	Sex (M/F)	Village / Town / IDP Camp	BCG (Date)	Polio (Date)	OPV (Date)				Pentavalent (Data) Talaalka gaviscatada iyo tetanuska			IPV (Date)		Pneumococcal (Date)			Rotavirus (Date)	Measles / MCV (Date)		Vitamin A Fitamiin A		Deworming (Dheeraynt)	Advese Event after Immunisation
Lambarka taxanaha ah	Taariikh booqashada kowaad	Taariik dhalashada / Da'da	Lambarka kaadhka ilmaha	Magaca oo Saddexan	Magaca hooyada ama mas'uulka / Telefoonka Gacanta	Jinsi (Lab/Dha)	Tuulada/Magaalada/Goobt a Barakacayaasha	Talaalka qaxarada	Talaalka dabeysha	OPV 0 (Birth / Dhalasho)	OPV 1	OPV 2	OPV 3	Pentavalent1	Pentavalent2	Pentavalent3	IPV 1	IPV 2	PCV 1	PCV 2	PCV 3	Rota dose ka 1aad	MCV 1 / Jadweca da	MCV 2 / Jadweca da	6-11 mn	12-59 mn	12-59 mn	Xanuun ansixiacdo kadib talaalka
A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC

Vitamin A	
6-11 months	
12-59 months	

Advese Event after Immunisation	
Deworming 12-59 months	

Annex III: AEFI reporting form

Federal Republic of Somalia
Ministry of Health & Human Services

REPORTING FORM FOR ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

Patient Serial No.:

***Patient Name:** _____

***Patient's Residence:** _____

***Mobile No:** _____ ***Sex:** _____ ***Date of birth *(DD/MM/YYYY)*:** __ /__ /__ __

***Health facility (or vaccination center) name:**

***Date of onset:**

Vaccine							*Diluent*		
Name of vaccine (Generic)	***Brand Name incl. name of manufacturer***	***Date of vaccination***	***Time of vaccination***	Dose (1st, 2nd, etc.)	***Batch/Lot number***	Expiry date	***Batch/ Lot number***	Expiry date	Time of reconstitution

Adverse event (s):

- ☐ Severe local reaction
- ☐ Seizures
- ☐ Abscess
- ☐ Sepsis
- ☐ Encephalopathy
- ☐ Toxic shock syndrome
- ☐ Thrombocytopenia
- ☐ Anaphylaxis
- ☐ Fever≥38°C
- ☐ >3 days ☐ beyond the nearest joint
- ☐ febrile ☐ afebrile
- ☐ OTHER (specify).....

***Date AEFI started** (DD/MM/YYYY): __ __ / __ __ / __ __ __ ***Time AEFI:** ..... Hr..... Min

***Serious: Yes / No;** ☐ If yes ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital anomaly _____

☐ Other important medical events (Specify _____

***Outcome:** ☐ Recovering ☐ Recovered ☐ Recovered with sequelae ☐ Not Recovered ☐ Unknown

☐ Died If died, date of death (DD/MM/YYYY): __ __ / __ __ / __ __ __ __ Autopsy done: ☐ Yes ☐ No ☐ Unknown

Past medical history of allergies or similar reactions: (dates and products).....

Describe concomitant Disease/Chronic Disease .....

Describe any medicine used one week before vaccine administration (Dose/Date of start/ending)

.....

Reporter's particulars

***Printed Name of Reporter:**

***Signature of reporter:**

***Date reported** (dd/mm/yy):

***Contact no:** _____

***Email address:** _____

Profession: ___MD ____ Ph ___NRN____Patient _____

Address: Corso Somalia Street, Shangani, Mogadishu, Somalia,
Send form to: Mobile No.+252 615906155, **Email:** abdinourst@gmail.com

Annex IV: AEFI investigation form

AEFI INVESTIGATION FORM

(Only for Serious Adverse Events Following Immunization – Death / Disability / Hospitalization / Cluster)

Section A **Basic details**

Province/State **District** **Case ID**

Place of vaccination (✓): ☐ Govt. health facility ☐ Private health facility ☐ Other (specify) _____
Vaccination in (✓): ☐ Campaign ☐ Routine ☐ Other (specify) _____

Address of vaccination site:

Name of Reporting Officer:

Date of investigation: __ __ / __ __ / __ __ __ __
Date of filling this form: __ __ / __ __ / __ __ __ __

Designation / Position:

This report is: ☐ *First* ☐ *Interim* ☐ *Final*

Telephone # landline (with code): Mobile: e-mail:

Patient Name

Sex: ☐ M ☐ F

(use a separate form for each case in a cluster)

Date of birth (DD/MM/YYYY): __ __ / __ __ / __ __ __ __

OR *Age at onset:* __ __ *years* __ __ *months* __ __ __ *days* ***OR*** *Age group:* ☐ *< 1 year* ☐ *1–5 years* ☐ *> 5 years*

Patient's full address with landmarks *(Street name, house number, locality, phone number etc.)*:

Name of vaccines/diluent received by patient	Date of vaccination	Time of vaccination	Dose (e.g. 1st, 2nd, etc.)	Batch/Lot number	Expiry date
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent
				Vaccine	Vaccine
				Diluent	Diluent

Type of site (✓) ☐ Fixed ☐ Mobile ☐ Outreach ☐ Other _____

Date of first/key symptom *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __ Time of first symptom *(hh/mm)*: __ __ / __ __
Date of hospitalization *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __
Date first reported to the health authority *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __

Status on the date of investigation (✓): ☐ Died ☐ Disabled ☐ Recovering ☐ Recovered completely ☐ Unknown

If died, date and time of death *(DD/MM/YYYY)*: __ __ / __ __ / __ __ __ __ *(hh/mm)*: __ __ / __ __
Autopsy done? (✓) ☐ Yes (date)_____ ☐ No ☐ Planned on (date)_____ Time_____
Attach report (if available)

Section B **Relevant patient information prior to immunization**

Criteria	Finding	Remarks (If yes provide details)
Past history of similar event	Yes / No / Unkn	
Adverse event after previous vaccination(s)	Yes / No / Unkn	
History of allergy to vaccine, drug or food	Yes / No / Unkn	
Pre-existing illness (30 days) / congenital disorder	Yes / No / Unkn	
History of hospitalization in last 30 days, with cause	Yes / No / Unkn	
Patient currently on concomitant medication? (If yes, name the drug, indication, doses & treatment dates)	Yes / No / Unkn	
Family history of any disease (relevant to AEFI) or allergy	Yes / No / Unkn	

For adult women
- Currently pregnant? Yes (weeks) _____ / No / Unknown
- Currently breastfeeding? Yes / No

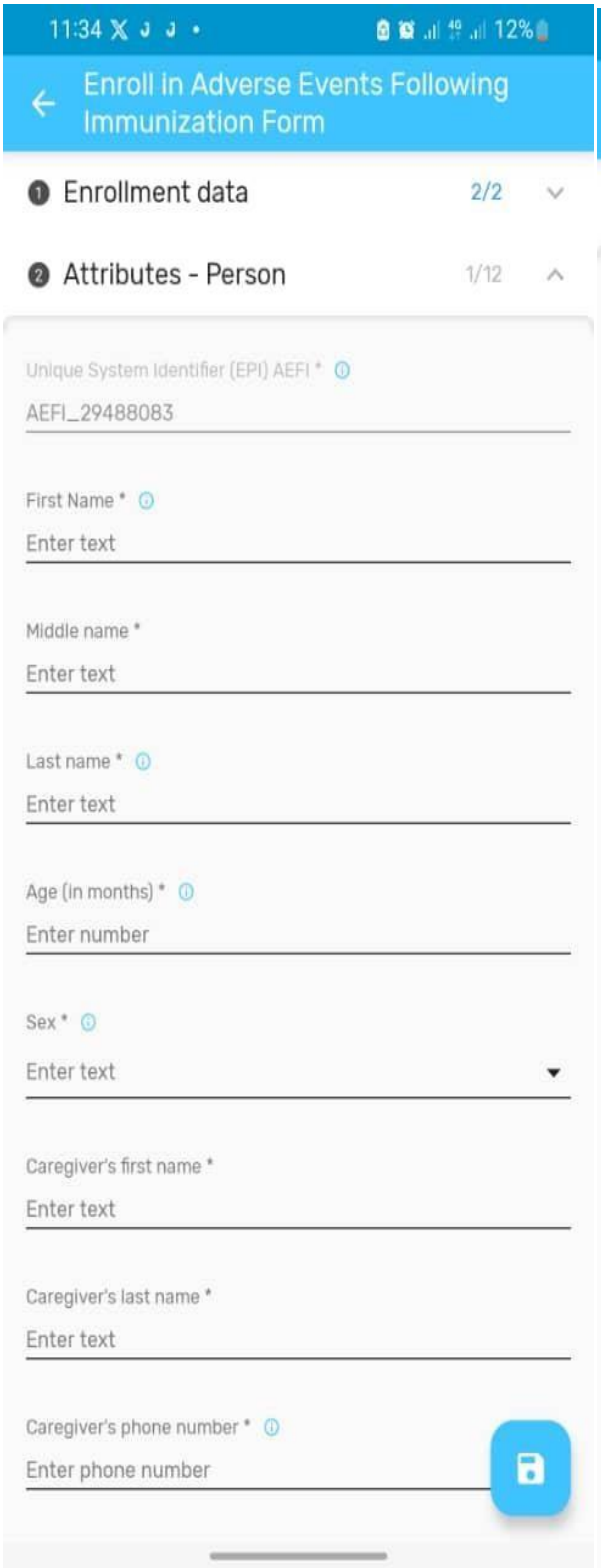
For infants
The birth was ☐ full-term ☐ pre-term ☐ post-term. Birth weight:

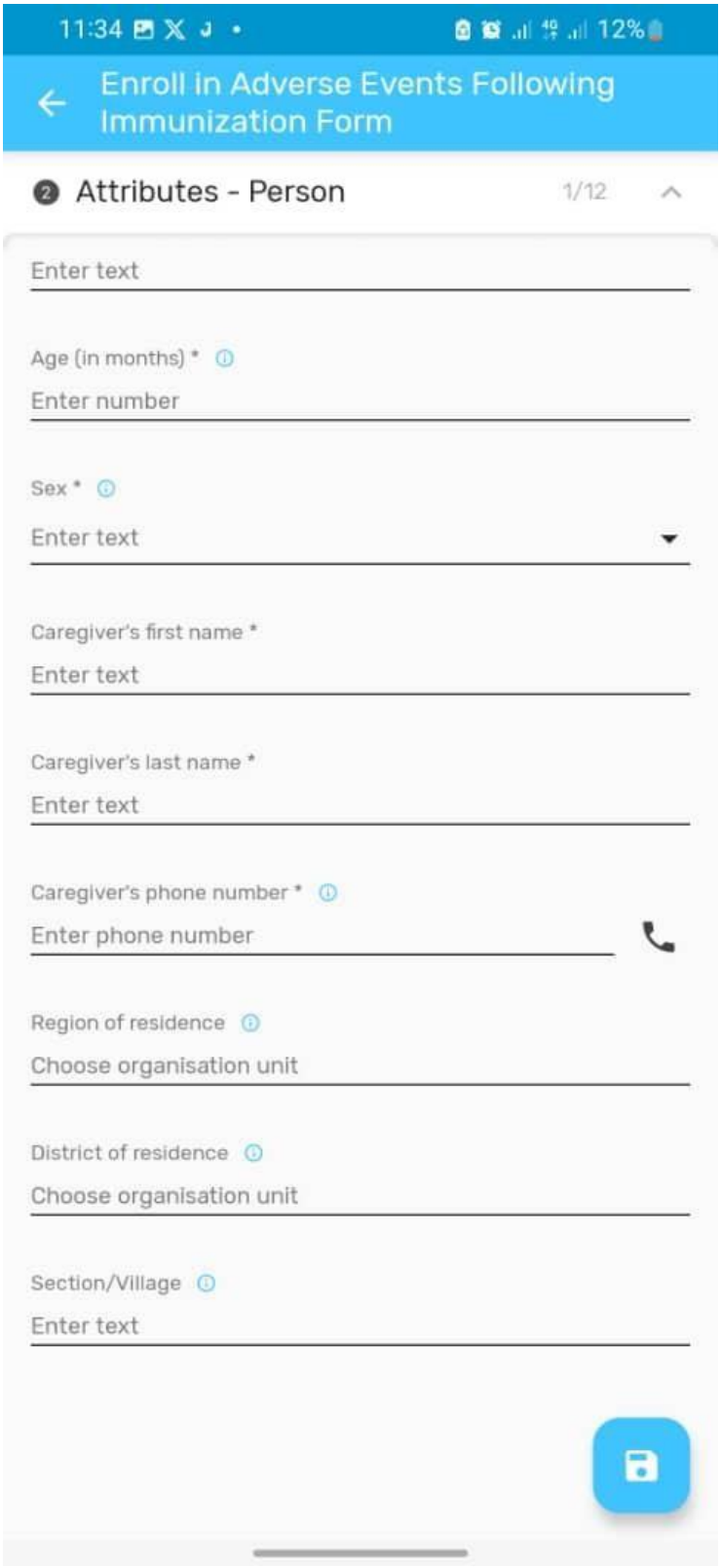
Delivery procedure was ☐ Normal ☐ Caesarean ☐ Assisted (forceps, vacuum etc.) ☐ with complication (specify)

Annex V: WHO-UMC causality assessment scale

Causality term	*Assessment criteria*
Certain	Event or laboratory test abnormality, with plausible time relationship to drug intake Cannot be explained by disease or other drugs Response to withdrawal plausible (pharmacologically, pathologically) Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) Rechallenge satisfactory, if necessary
Probable / Likely	Event or laboratory test abnormality, with reasonable time relationship to drug intake Unlikely to be attributed to disease or other drugs Response to withdrawal clinically reasonable Rechallenge not required
Possible	Event or laboratory test abnormality, with reasonable time relationship to drug intake Could also be explained by disease or other drugs Information on drug withdrawal may be lacking or unclear
Unlikely	Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) Disease or other drugs provide plausible explanations
Conditional / Unclassified	Event or laboratory test abnormality More data for proper assessment needed, or Additional data under examination
Unassessable / Unclassifiable	Report suggesting an adverse reaction Cannot be judged because information is insufficient or contradictory Data cannot be supplemented or verified

Annex: VI: IDSR-AEFI data entry form





GLOSSARY OF TERMS

Active safety surveillance: Active safety surveillance (or *Active Pharmacovigilance*) is an active system for detecting adverse events. This is achieved by active follow-up after vaccination. Events can be detected by asking patients directly or by screening patient records. It is best done prospectively.

Adjuvant:A pharmacological or immunological agent added to a vaccine to improve its immune response.

Adverse drug reaction (ADR):This is a response to a medicine that is noxious and unintended and occurs at doses normally used in man.
In this description, it is important that it concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).

Adverse event (AE): Any untoward medical occurrence that may present during treatment with a medicine or vaccine but does not necessarily have a causal relationship with this treatment.
The basic point here is the coincidence in time without any suspicion of a causal relationship.

Adverse event following immunization (AEFI): Any untoward medical event that follows immunization and does not necessarily have a causal relationship with the usage of the vaccine. For example, the adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease.
Depending on the cause, they can be classified as:

- *Coincidental events* — An AEFI caused by something other than the vaccine product, immunization error or immunization anxiety.
- *Immunization anxiety-related reaction*— An AEFI arising from anxiety about the immunization (see immunization stress-related responses). See also *Immunization stress-related response*.
- *Immunization error-related reaction* — An AEFI caused by inappropriate vaccine handling, prescribing or administration that is preventable.
- *Vaccine product-related reaction* — An AEFI caused or precipitated by a vaccine due to one or more of the inherent properties of the vaccine product, whether the active component or one of the vaccine's other components (e.g. adjuvant, preservative or stabilizer).
- *Vaccine-quality defect-related reaction* — An AEFI caused or precipitated by a vaccine due to one or more quality defects of the vaccine product, including its administration device as provided by the manufacturer.

Adverse event of special interest(AESI): A preidentified and predefined medically-significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further specific studies.

Causal association: A cause-and-effect relationship between a causative (risk) factor and an outcome. The causal association is determined during the investigation process of any report by assessing the following:

- the temporal relationship between the administration of the medicine or vaccine and the first symptoms of the AE;
- the medical and pharmacological plausibility;
- what happens after discontinuing the medicine;
- what happens after a reexposure (if there is reexposure);
- if all alternative causes have been dismissed.

Usually, the causal association is established by using a *Causality algorithm.*
Causally-associated events are also temporally associated (i.e. they occur after vaccine administration), but temporally associated events may not necessarily be causally associated.

Causality assessment: Systematic review of data about the reported case to determine the likelihood of a causal association between the event and the vaccine(s) received.

Causality algorithm: A series of questions that help to investigate the causal association systematically. There are many causality algorithms. The most commonly used are the Karch & Lasagna and the Naranjo. In the case of vaccines, the Brighton collaboration also defines the cases that can help.

Cluster: Two or more cases of the same or similar events related in time, geography (place), and/or vaccine administered.
AEFI clusters are usually associated with a particular supplier/provider, health facility, and/or a vaccine vial or batch of vaccines.
ADR clusters can be related to quality problems or, rarely, genetic or ethnic differences in susceptibility to specific medicines.

Confidentiality: Maintenance of the privacy of patients, healthcare providers and institutes, including personal identities and medical information.

Contraindication: A situation where a particular treatment or procedure must not be administered for safety reasons.
Contraindications can be permanent (absolute), such as known severe allergies to a vaccine component or medicines that can't be prescribed to patients with liver failure, or temporary (relative), such as an acute/severe febrile illness.

Drug: See *Medicine*

Drug safety: Safety of medicines. This includes all processes, research and actions for the early detection of the profile of adverse reactions to medicines and vaccines, studies to identify and quantify risks and interventions to spread that knowledge and minimize future risks. Pharmacovigilance based on spontaneous reporting is the most common drug safety activity conducted at the national level.

Efficacy: Ability of a medicine or medical technology to bring about the intended beneficial effecton individuals in a defined population with a given medical problem under ideal conditions of use. Clinical trials show efficacy.

Immunization: Process whereby a person is made immune or resistant to infection, typically by administering a vaccine. Vaccines stimulate the body's immune system to protect the person against subsequent infection.

*Immunization safety*The process of ensuring the safety of all aspects of immunization, including vaccine quality, adverse event surveillance, vaccine storage and handling, vaccine administration, disposal of sharps and management of waste.

Immunization safety surveillance: Pharmacovigilance activities focused on the use of vaccines. A system for ensuring immunization safety through early detection, reporting, investigating, and quickly responding to AEFIs.
Immunization stress-related responses (ISRR): Stress response to immunization that may manifest just before, during, or after immunization. It is also called immunization anxiety.

Individual case safety reports (ICSRs): Reports of suspected ADR or AEFI that have been evaluated and comply with the minimum requirements and are included in the database.

Injection safety: The public health practices and policies dealing with various aspects of the use of injections (including adequate supply, administration and waste disposal) so that the provider and recipient are not exposed to avoidable risks of adverse events (e.g. transmission of infective pathogens) and creation of dangerous waste is prevented. All injections, irrespective of their purpose, are covered by this term (see definition of safe injection practices).

*Medicine***:** is a pharmaceutical product used in or on the human body for the prevention, diagnosis or treatment of disease or the modification of physiological function.

Non-serious ADR or AEFI: An event that is not 'serious' and does not pose a potential risk to the recipient's health.
Non-serious ADR associated with new medicines should also be carefully monitored because, at this stage, the medicine's safety profile is being studied.
Non-serious AEFI should also be carefully monitored because they may signal a potentially larger problem with the vaccine or vaccination or impact vaccination acceptability.

Passive Pharmacovigilance(also *Spontaneous or Voluntary reporting): Pharmacovigilance based on reporting* adverse events to the pharmacovigilance system. *Note that reporting is compulsory for manufacturers.*

Pharmacovigilance (PV): Discipline and activities which object is the surveillance, assessment, prevention and management of the risk of unwanted effects (side effects, adverse drug reactions) as the result of the prescription, administration and use of medicines, vaccines and other medicinal products or herbal remedies.

Pharmacovigilance system: A PV System is used by the Ministry of Health to fulfil its legal tasks andresponsibilities concerningPharmacovigilance, designed to monitor the safety of authorizedmedicinal products (and any other medicine taken by patients) and detect any change to their risk-benefit balance.

Post-marketing surveillance: Monitoring for adverse reactions to marketed products. It includes passive Pharmacovigilance (spontaneous reporting), active Pharmacovigilance and other observational studies.

Report: Communication of an adverse event after taking a medicine or vaccine. It is the primary communication of the reporter (healthcare professional or citizen) and the Pharmacovigilance system. It is made using the official *Reporting Form*.

Reporting form: It is an official document used by the Pharmacovigilance System to receive reports of adverse events.
The information to be filled in the reporting form is concise; it includes minimal variables to perform the causality assessment.
It is very important that the information in the report is accurate and that all the information is filled in, especially dates, concomitant medication and conditions, and tests to discard alternative causes.

Risk management plan (RMP):The risk management plan is a document established by the vaccine manufacturer that contains the following elements:

a) identification or characterization of the safety profile of the medicinal product(s) concerned;
b) indication of how to characterize the safety profile of the medicinal product(s) concerned further;
c) documentation of measures to prevent or minimize the risks associated with the medicinal product, including an assessment of the effectiveness of those interventions;
d) documentation of post-authorization obligations imposed as a condition of the marketing authorization.

Serious adverse events: Those AEs that: (a) are life-threatening or fatal; (b) cause or prolong hospital admission; (c) cause persistent incapacity or disability; or (d) concern misuse or dependence.
Any medical event that requires intervention to prevent one of the outcomes above may also be considered serious.

Severe/Severity: The term "severe" is not synonymous with serious in this context. Severe describes a specific event's intensity (severity) (For example, mild, moderate or severe myocardial infarction).
For example: "Severe vaccine reaction". Vaccine reactions can be mild, moderate or severe based on their intensity. The event itself, however, may be of relatively minor medical significance. Severe events do not have regulatory implications unless they are also serious.

Side effect: Any unintended effect of a pharmaceutical product occurring at doses normally used in man, which is related to the pharmacological proprieties of the drug.
Essential elements in this definition are the pharmacological nature of the effect, the phenomenon is unintended, and there is no overt overdose.

Signal: Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously.
Usually, more than a single report is required to generate a signal, depending upon the event's seriousness and the information's quality.
In these definitions, drug or drug-food interactions are also included. It should be added that many patients have only suspected adverse reactions in which the causal role of the drug is unproven and may be doubtful and that pharmacovigilance data usually refer to only suspected adverse reactions and side effects.

Spontaneous reporting: see Passive Pharmacovigilance.

Surveillance: The continual, systematic collection of data that are analyzed and disseminated to enable decision-making and action to protect the health of populations.
Type A effects ('drug actions') are due to (exaggerated) pharmacological effects.
Type A effects tend to be fairly common and dose-related (i.e. more frequent or severe with higher doses) and may often be avoided by using appropriate doses for the individual patient. In addition, such effects can usually be reproduced and studied experimentally and are often already identified before marketing.
Interactions between drugs, especially pharmacokinetic interactions, may often be classified as Type A effects. Again, however, they are restricted to a defined sub-population of patients (i.e. the users of the interacting drug).

Type B effects('patient reactions') characteristically occur in only a minority of patients and display little or no dose relationship. They are generally rare and unpredictable, may be serious and are notoriously difficult to study.
Type B effects are either immunological or non-immunological and occur only in patients with - often unknown - predisposing conditions. Immunological reactions may range from rashes, anaphylaxis, vasculitis, and inflammatory organ injury, to highly specific autoimmune syndromes. Also, non-immunological Type B effects occur in a minority of predisposed, intolerant patients,e.g. because of an inborn error of metabolism or acquired deficiency in a certain enzyme, resulting in an abnormal metabolic pathway or accumulation of a toxic metabolite. Examples are chloramphenicol, aplastic anemia and isoniazid hepatitis.

Type C effects refer to situations where drug use increases the frequency of 'spontaneous' disease, often for unknown reasons.
Type C effects may be both serious and common (and include malignant tumors) and may have pronounced effects on public health.
Type C effects may be coincidental and often concern long-term effects; there is often no suggestive time relationship, and the connection may be difficult to prove.

Unexpected ADR: is 'an adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization, or expected from characteristics of the drug'. Here the predominant element is that the phenomenon is unknown.

Vaccine: A biological preparation that elicits immunity to a particular disease. In addition to the antigen, it can contain multiple components, such as adjuvants, preservatives, and stabilizers, each of which may have specific safety implications.

Vaccination failure:Vaccination failure can be defined based on clinical endpoints or immunological criteria where correlates or surrogate markers for disease protection exist. Primary failure (e.g. lack of seroconversion or seroprotection) must be distinguished from secondary failure (waning immunity).
Vaccination failure can be due to (i) failure to vaccinate, i.e. an indicated vaccine was not administered appropriately for any reason or (ii) because the vaccine did not produce its intended effect.

Validation: The action of proving that any procedure, process, equipment (including the software or hardware used), material, activity or system used in Pharmacovigilance leads to the expected results.

Verification: The procedures carried out in Pharmacovigilance to ensure that the data contained in a final report matches the original observations. These procedures may apply to medical records, data in case-report forms (in hard copy or electronic form), computer printouts, and statistical analyses and tables.

VigiBase: WHO global database of individual case safety reports (ICSRs), including ADRs and AEFIs, maintained by the Uppsala Monitoring Centre.

VigiFlow: A web-based individual case safety report (ICSR) management system (E2B compatible) for medicines and vaccines developed and maintained by Uppsala Monitoring Centre.

Voluntary reporting: see *Passive Pharmacovigilance.*