REPUBLIC OF RWANDA

MINISTRY OF HEALTH

Guidelines for Pharmacovigilance and Medicine Information in Rwanda

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FOREWORD

On June 26, 2010, the Food and Medicines Act developed by the Ministry of Health was approved. It identifies the Rwanda Food and Medicines Authority (RFMA) as the regulatory board of all medicine and food related issues. This document has been submitted to the country's high authorities for approval. One of the RFMA's core mandates is to ensure that the medicines used in the country are of good quality, safe and efficacious.

As the RFMA is not yet established, the Ministry of Health has entrusted this to the Directorate of Clinical Services which performs most activities related to pharmaceutical regulations, among them Pharmacovigilance and medicine information.

Medicines, despite their obvious benefits, can also cause adverse drug reactions (ADRs) which can be serious or even fatal. ADRs must be reported and analyzed to protect the public health and improve the patient care.

These guidelines for the National Pharmacovigilance and Medicine Information System in Rwanda have been developed to ensure that safe, efficacious and quality medicines are made available to all Rwandans.

I acknowledge the contribution of different units, departments and divisions in the Ministry of Health (MoH) and Rwanda Biomedical Center (RBC); the National University of Rwanda (NUR), the World Health Organization in Rwanda and the Management Sciences for Health's Strengthening Pharmaceutical Systems (SPS) Program office in Kigali.

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Minister of State in Charge of Public Health and Primary Health Care

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ACRONYMS AND ABBREVIATIONS

AE	Adverse Event
ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
CHW	Community Health Worker
DTC	Drug and Therapeutics Committee
GoR	Government of Rwanda
HIV	Human Immunodeficiency Virus
MAH	Marketing authorization holder
MoH	Ministry of Health
NMSC	National Medicine Safety Committee
MSH	Management Sciences for Health
NMRA	National Medicine Regulatory Authority
NPMIC	National Pharmacovigilance and Medicine Information Center
PHP	Public Health Program
PTF	Pharmacy Task Force
RFMA	Rwanda Food and Medicines Authority
SOP	Standard Operating Procedures
SPS	Strengthening Pharmaceutical Systems [Program]
TB	Tuberculosis
TRAC	Treatment and Research AIDS Center
UMC	*The* Uppsala Monitoring Centre
WHO	World Health Organization

INTRODUCTION

The need for monitoring medicines safety is globally recognized. Pre-marketing clinical trials for the evaluation of quality, efficacy, and safety of new medicines provide the first opportunity for generating data on the safety of a new medicine. However, pre-market clinical trials have many limitations, including the relatively few number of patients exposed and lack of complete understanding of long-term effects, co-morbid conditions, and use in the elderly, children, and pregnant women, and among different racial groups. This means that when a new medicine is released to the public, comprehensive understanding of its safety profile is incomplete.

Additionally, there have been increased efforts recently to expand access and introduce new pharmaceutical products in developing countries. The Government of Rwanda (GoR) has ensured access to these new pharmaceutical products for the management of HIV/AIDS, tuberculosis (TB) and malaria. There is now a great need to compliment the efforts at expanding access with adequate attention to rational use and safety monitoring. Monitoring safety during real-life use can provide valuable safety information to compliment safety data generated during pre-marketing clinical trials.

The need for safety monitoring may be particularly important in resource-constrained countries. Adverse drug reactions (ADR) rank among the top 10 leading causes of mortality in several developed countries;[1] the overall incidence of serious ADRs from 1966 to 1996 was 6.7 percent in the United States and the United Kingdom.[2] The burden of ADRs in Rwanda is unknown; however, it is projected that the burden may even be higher due to several factors including—

- High prevalence of HIV/AIDS, TB, malaria and other co-morbid conditions
- Insufficient knowledge of the quality of pharmaceutical products
- Widespread use of traditional and complimentary medicines
- Different genetic and nutritional status of Rwandese compared to those individuals who participated in the clinical trials
- Lack of capacity to monitor for early signs of toxicity

Pharmacovigilance and medicine information systems are therefore required in Rwanda. Pharmacovigilance can provide useful information when characterizing and quantifying previously recognized ADRs, determining actual effectiveness, identifying, and preventing new drug-induced diseases early on, and reducing mortality and morbidity.

Traditional medicine use is increasing in the Western world (where it is not well regulated) and is widespread in African countries. Several herbal medicines are used frequently, and may be associated with adverse effects. Continuing vigilance is needed.[3]

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[1] Safety of Medicine -A guide to detecting and reporting adverse drug reaction- why health professionals need to take action. http://apps.who.int/medicinedocs/en/d/Jh2992e/

[2] Lazarou, J, B. H. Pomeranz, and P.N. Corey. 1998. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *Journal of the American Medical Association* 279:1200-5.

[3] *The* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. 2000. World Health Organization. 2000. Safety Monitoring Of Medicinal Products. Guidelines for Setting Up and Running a Pharmacovigilance Centre. [in French]. Geneva: WHO.

The Rwanda Ministry of Health (MoH) is committed to improving medicine safety monitoring and protecting the public health. Guidelines and regulations are in place to ensure that the safety and effectiveness of medicines available in Rwanda are monitored. It is the vision of the MoH that all such related activities should be standardized and coordinated. These *Guidelines for Pharmacovigilance and Medicine Information System in Rwanda* provide standard operating procedures (SOPs) and directions for addressing all issues related to medicines and patient safety in a comprehensive manner. Users are encouraged to regularly refer to these guidelines for consistent understanding of medicine safety surveillance activities in Rwanda.

Establishment of the National Pharmacovigilance and Medicine Information Center

To address the need of a system for routine medicine safety surveillance and to ensure the protection of public health, the Rwanda MoH has established the National Pharmacovigilance and Medicine Information Center (NPMIC). The NPMIC is based within the National Medicine Regulatory Authority (NMRA) in the MoH. The NPMIC will fulfill its medicine safety role by liaising with numerous MoH units, departments and committees.

Overarching goal of the NPMIC

NPMIC's goal is to develop and implement Pharmacovigilance and medicine information systems that will provide unbiased information, monitor safety and effectiveness and improve rational use of pharmaceutical products in Rwanda.

Scope of Pharmacovigilance and Medicine Information System in Rwanda

The scope of activities grouped under Pharmacovigilance and medicine information undertaken by NPMIC in Rwanda includes the following—

- Monitor safety, effectiveness and tolerability of medicines used in Rwanda
- Quantify and characterize occurrence of previously recognized ADRs in Rwanda
- Conduct and coordinate spontaneous reporting and active surveillance activities
- Provide unbiased medicine information to health workers and consumers
- Monitor the promotion and advertising of all health products
- Improve rational medicines use
- Contribute to patient safety improvement
- Develop interventions to reduce pharmaceutical product-induced morbidity and mortality

In addition, there are several MoH committees that are responsible for ensuring participation in medicine safety surveillance activities, such as the selection of medicines for inclusion in the standard treatment guidelines or the essential medicines lists. Information on safety, comparative

effectiveness and rational medicines use greatly influence medicines selection activities like the development of standard treatment guidelines, the clinical practice guidelines and the national essential medicines list. The NPMIC is a national resource in providing evidence-based information to influence medicines selection and related activities of technical committees in Rwanda working in these areas.

Importance of Pharmacovigilance

The World Health Organization (WHO) defines Pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. Recently, its concerns have been widened to include[4]—

- Herbal medicines
- Traditional and complementary medicines
- Blood products
- Biologicals
- Medical devices
- Vaccines

The information collected during the pre-marketing phase of drug development is inevitably incomplete with regards to possible ADRs. This is mainly because—

- Tests in animals are insufficiently predictive of human safety

- In clinical trials, patients are selected and limited in number, the conditions of use often differ from those in clinical practice and the duration of trials is limited

- Information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available

For all medicines, there is a tradeoff between the benefits and the potential to harm. To minimize the harm, it is necessary that medicines of good quality, safety and efficacy are used rationally and that the expectations and concerns of the patient are taken into account when therapeutic decisions are made.

Importance of Unbiased Medicine Information

The provision of easily accessible and reliable unbiased information on medicines is an essential element in achieving national health goals in Rwanda. Medicine information service is committed to provide information to health care professionals, patients and/or consumers[4] and will be useful in the following situations—

- Improving care and treatment outcomes
- Ensuring that only evidence-based, consistent and locally peer-reviewed information are provided to health workers and consumers
- Providing health workers and consumers information on safety of medicines obtained from credible sources
- Educating health workers and consumers through trainings, written materials, and other media activities
- Monitoring medicine promotion and advertising activities to identify and address spurious claims and misinformation
- Conducting comparative effectiveness reviews
- Providing pharmaceutical-related information to other MoH technical committees involved in pharmaceutical products

[4] U.S. Pharmacopeia. USP DQI Drug Information Program. (program title change, now known as "Promoting the Quality of Medicines"). Available at http://www.usp.org/worldwide/PQMResourceLibrary.html

ADVERSE EVENT NOTIFICATION SYSTEM FOR PHARMACOVIGILANCE

An adverse event (AE) is any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with the treatment. An adverse drug reaction (ADR) is a response to a medicine which is noxious and unintended, and occurs at a dose normally used in humans for prophylaxis, diagnosis or therapy of disease; or for the modification of physiological function. This means that any ADR is included in adverse event.

In Rwanda, the notification system focuses on detection of adverse events and the NPMIC together with the Pharmacovigilance subcommittees in hospitals conduct causality assessment in order to ensure that this event was really an ADR.

Reporting system

NPMIC activities rely heavily in regular interactions with healthcare providers and the patients/consumers. Figure 1 shows the AE reporting system developed to guide the flow of information for all the activities under the scope of the Pharmacovigilance system. A Pharmacovigilance concern or a request for medicine information originates with the patient or consumer. The patient/consumer is at the very foundation of the Rwandan reporting system. The patient/consumer can report adverse events and/or request for medicine information through ant healthcare provider present in health posts, health centers, private sector clinics and pharmacies, hospitals and community health workers (CHW). All adverse events communicated by the patient/consumer will be reported through an adverse event notification form filled in by healthcare providers and collected by the respective hospital Pharmacovigilance subcommittees (which serve as the hub for the implementation of Pharmacovigilance activities). The NPMIC has collaborative responsibilities with several bodies including the public health programs and the technical committees (for example, the standard treatment guidelines committees and the pharmaceutical products list committee). The NPMIC reports to the NMRA which is accountable to the MoH.

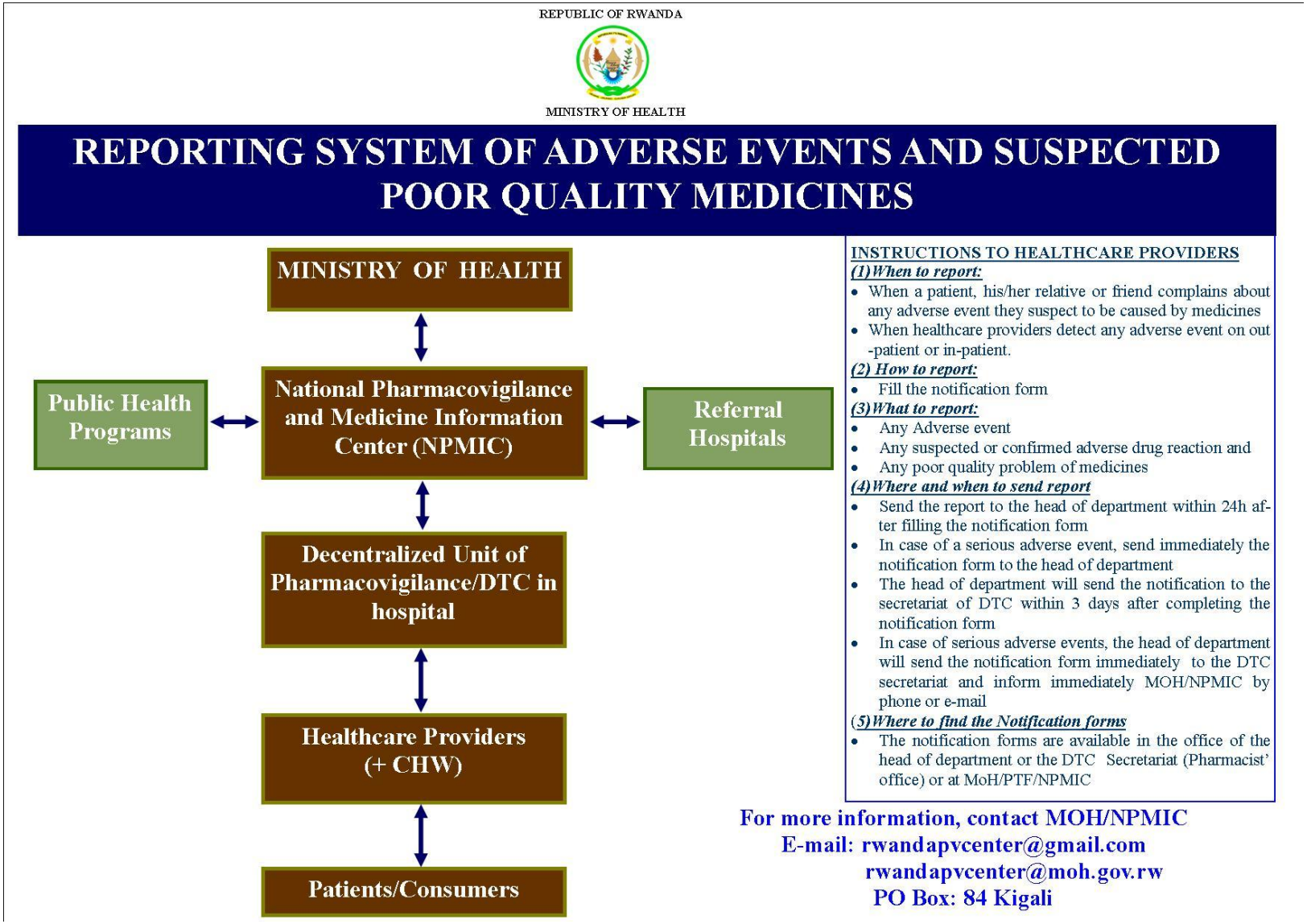


Figure 1. Rwandan reporting system

Roles and responsibilities in relation to Pharmacovigilance and Medicine Information

It is important that all stakeholders, consumer organizations, civil societies and the public have roles in monitoring safety and rational medicines use in Rwanda. The public are therefore encouraged to participate in Pharmacovigilance activities through the channels of the notification system. The roles and responsibilities of all bodies listed in the adverse event notification system are listed below.

Patient/Consumer

Patients/consumers have the following roles in medicine safety surveillance in Rwanda—

- If a patient/consumer, family member, or someone the client knows experiences an adverse event occurring during/after any medication or medical intervention, the event should be reported to a healthcare provider

- Request information from the healthcare providers within the health facilities or directly from the NPMIC concerning any medicine

- Report any suspicion of poor quality medicine to the community health workers, health posts, health centers, hospitals, private clinics and pharmacies, or directly to the NPMIC

Healthcare providers including Community Health Workers

The healthcare providers provide the best quality care to patients. One of the responsibilities of healthcare providers is to encourage patients to ask questions about their health condition and to report adverse events. When patients report adverse events, healthcare providers have to manage and report those adverse events.

Reporting these adverse events will provide valuable national data to be used by technical committees and orient the regulatory decisions. Healthcare providers have the following roles and responsibilities—

1. Provide advice to the patients on the need to adhere to the treatment plan and to report any adverse event

2. Detect and manage adverse events and all health product-induced disorders

3. Report all adverse events to the NPMIC through Pharmacovigilance subcommittees

4. Participate in Pharmacovigilance activities in collaboration with the subcommittees

Note: In case of health products adverse events communicated to community health workers, the workers have the responsibility to refer the patient to the health post/centre for further care and report the event.

PV Subcommittees

Among the Drug and Therapeutics Committee (DTC) members, a subcommittee is appointed to serve as the Pharmacovigilance subcommittee. This DTC subcommittee has to implement the policies, guidelines and standards of the NPMIC. It has the following responsibilities—

- Implement the *Guidelines for Pharmacovigilance and Medicine Information System* in health facilities within its catchment area.
- Ensure the availability of the adverse event notification forms and patient alert cards in health facilities
- Collect, validate and transmit all notifications to NPMIC
- Ensure that healthcare providers are trained and familiar with the completion of the notification forms and patient alert cards
- Sensitize healthcare providers on Pharmacovigilance activities
- Collaborate regularly with the NPMIC on Pharmacovigilance and medicine information related issues
- Identify and suggest interventions to address any medicine safety and/or irrational use issues in health facilities within their catchment area

Public Health Programs

The public health programs (PHPs) are sometimes requested to use new essential medicines. In addition, PHPs which include mass treatment programs, do not have qualified healthcare providers at community level. In these regards, public health programs are expected to be sensitive to medicine safety issues. The PHPs, therefore, have the following responsibilities—

- Collaborate with NPMIC to identify priority safety issues related to medicines used in their programs
- Collaborate with NPMIC to identify, plan and conduct active surveillance studies to provide more information on safety issues related to medicines used in the program
- Organize formal reporting of adverse events in mass treatment campaigns
- Help increase awareness on the need to report adverse events for their particular products and their transmission to the NPMIC
- In collaboration with NPMIC, work with the Rwanda National Ethics Committee and other related bodies to ensure proper review of study protocols

- Provide findings on all medicine safety-related studies to the NPMIC
- Provide regular feedback to NPMIC on selected medicines safety indicators
- Collaborate with NPMIC to provide regular trainings on Pharmacovigilance for health care providers in the PHPs
- Collaborate with NPMIC in using the standard operating procedures (SOPs) and initiating active surveillance of the medicines they manage

NPMIC

To fulfill the goal of developing and implementing the Pharmacovigilance and medicine information system, the NPMIC has the following roles and responsibilities—

- Provide technical advice to the MoH authorities in all policy decisions related to medicine safety in Rwanda
- Provide technical advice to the NMRA and other related bodies for decision making
- Develop standards and procedures for Pharmacovigilance and medicine information activities in Rwanda
- Identify Pharmacovigilance and medicine information priorities and lead all efforts in addressing them
- Develop, implement and update tools for all Pharmacovigilance and medicine information activities
- Supervise all relevant Pharmacovigilance studies
- Coordinate in-service Pharmacovigilance educational activities for healthcare providers and consumers
- Coordinate and provide technical support to PV subcommittees
- Collaborate with the academic institutions and other stakeholders in providing pre-service trainings in Pharmacovigilance
- Provide medicine information to healthcare providers, patients/consumers and the entire public through telephone, internet, media and publications
- Conduct causality assessment on received adverse event notifications

- Serve as the secretariat of the National Medicine Safety Committee (NMSC)

- Collaborate and participate in regional and international activities related to Pharmacovigilance and medicine information

- Collaborate with the WHO/Uppsala Monitoring Centre (*the* UMC) and other Pharmacovigilance centers to exchange information and data related to medicine safety

- Establish formal ways of collaboration with all stakeholders in all issues related to Pharmacovigilance and medicine information

NMRA

The NMRA oversees the functioning of the NPMIC and has the following responsibilities—

- Supervise the implementation of the national *Guidelines for Pharmacovigilance and Medicine Information System*

- Identify knowledge and gaps in Pharmacovigilance and collaborate with the NPMIC to address them

- Propose to MoH the decisions to be taken to improve medicine safety surveillance and information.

NMSC

The National Medicine Safety Committee serves as an expert advisory committee to the Ministry of Health for Medicine safety, effectiveness and quality issues. It is a multidisciplinary committee composed of specialized individuals appointed by the Ministry of Health (MoH).

The NMSC has the following responsibilities:—

- Advise on Medicine registration issues related to safety, effectiveness and quality;

- Provide technical advice to the National Pharmacovigilance and Medicine Information Center (NPMIC) in causality assessment and/or analysis on medicine adverse events.

Other Stakeholders

Marketing Authorization Holders

Marketing authorization holders (MAHs) in Rwanda include the holder of the registration certificate, the local representative of the manufacturer (distributor or wholesaler), the importer of the product and all other persons who obtained permission from the NMRA to manufacture, import and market pharmaceuticals in Rwanda. Each MAH has the following responsibilities towards medicine safety surveillance in Rwanda—

- Mandatory reporting of all adverse events associated with the product the holder is authorized to distribute, including those events that are not detected in Rwanda. MAHs are responsible to report all such adverse event reports that they are informed of to the NPMIC. Serious adverse events should be reported within 48 hours of the receipt of such reports, while non serious events should be reported within 15 days of the receipt of the report. The MAH can use the NPMIC notification form for the purpose of this report

- The MAH is expected to provide all medicine safety relevant information related to his or her authorized product to the NPMIC every three months

- The MAH who intends to promote and advertise products or provide sponsorships should adhere to the regulation in place.

- MAHs should collaborate with the NPMIC toward conducting post-authorization safety studies as identified by relevant authorities in Rwanda

There are many stakeholders that will need to be involved in the national Pharmacovigilance and medicine information system at different levels, such as qualified health professionals, researchers and academic institutions, media, procurement agencies, standardization institutions, funding and technical assistance partners, and international and regional health organizations.

UMC/WHO

The UMC's responsibilities in regards to the national Pharmacovigilance centers, including the NPMIC, are globally the same.

- Receive and store reports from national Pharmacovigilance centers

- Provide tools, trainings and access to information systems to enable national Pharmacovigilance centers to search the global WHO database

- Monitor signals from the global WHO database (a signal refers to "reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously.")

- Communicate signal analyses to national Pharmacovigilance centers and clinical review of the analyses by experts
- Provide technical assistance to national Pharmacovigilance centers
- Facilitate communication between countries
- Develop and maintain WHO Adverse Reaction Terminology and the use of the Medical Dictionary for Regulatory Activities within the WHO International Drug Monitoring Program
- Train national Pharmacovigilance centers' staff
- Standardize procedures relating to Pharmacovigilance activities
- Publish relevant documents
- Provide data as appropriate to other parties

A signal refers to "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 seriousness of the event and the quality of the information.

MEDICINE INFORMATION

Literature scan for relevant safety alerts

The NPMIC shall provide unbiased and evidence-based medicines information to health care professionals, consumers and the public. Appropriate medical literature will be routinely scanned for relevant safety alerts which will then be communicated to stakeholders.

Risk communication

The NPMIC shall communicate the risk related to medicine safety guided by the risk communication manual for medicine safety.

Requesting medicine information

Healthcare professionals, consumers and the public should request medicine information from the NPMIC. Medicine information provided by the NPMIC should be independent and evidence-based. The NPMIC should establish a quality assurance system to ensure that quality medicine information is provided.

Information, Education, Communication Materials and NPMIC Publications

The NPMIC shall routinely produce relevant information, education, communication materials to meet its objective towards providing quality, relevant and evidence-based medicine information. The NPMIC shall maintain a regular publication of medicine information and medicine safety bulletin or newsletter.

Medicine Promotion and Advertising

All medicine promotion and advertising activities shall be conducted with a primary aim of promoting public health and according to the regulations in place. The NPMIC shall notify the competent authority of any medicine promotion and advertising activities that can negatively impact on patient and medicines safety.

The national guidelines for promotion and advertising of pharmaceutical products shall be adapted by the NMRA with guidance from the WHO ethical criteria.

PHARMACOVIGILANCE METHODS

The classic Pharmacovigilance system relies on[5]—

- Passive surveillance: This applies to the entire population and monitors any adverse events that occur in any patient. Among its weaknesses, there are lack of solid comparisons (target and subject of the surveillance) and the inaccuracy of reporting in addition to the low rate of occurring events. It generates signal/alert that active surveillance could use for further investigations.

- Active surveillance: This method uses the pharmaco-epidemiological methods to overcome the limitations of the passive Pharmacovigilance. Based on the signal/alert generated by passive surveillance, it helps to identify the subject of surveillance and applies an appropriate methodology that will allow the causality assessment of adverse event. Its main weakness is its high cost in addition to its limited number of subjects.

- MAH surveillance: Once a product is authorized to be on the market, the MAHs are requested to continue to closely monitor their product's safety to contribute post marketing surveillance. This surveillance combines both passive and active surveillances and it is initiated by the MAHs without any direct participation of the NPMIC.

Passive surveillance is the principal method adapted to limited resources settings like Rwanda. As spontaneous reporting is known as the basic mechanism of this surveillance, it is the main method to be used in generating signals/alerts of adverse events for further investigations.

Spontaneous Reporting

Spontaneous reporting involves the submission of unsolicited adverse event reports to NPMIC. This is useful for identifying safety signals of rare adverse reactions and generating hypotheses. It provides critical information that is in identifying patients who are at risk of an adverse effect to a medicine. It also can give more information on real-life experience with a medicine beyond data obtained from clinical trials.

Spontaneous reports are usually submitted in standardized notification forms that include four key fields—patient identification, adverse event, suspected product and details on the healthcare professional who produced the adverse event report. Other details, however, must also be reported to help the causality assessment like allergies to medications, other risk factors, etc.

Spontaneous reports can be used for to the reporting of all known and undocumented (unknown) adverse events, serious or not. These events could be the consequences of medication errors, drug interactions, therapeutic ineffectiveness, product quality problems, and problems with medical devices even if there is no obvious relationship between the event and the suspected product. It is important to send spontaneous reports to the NPMIC promptly.

[5] WHO. 2002. *Safety of Medicines. A guide to detecting and reporting adverse drug reaction; why health professionals need to take action*. Geneva: WHO. http://whqlibdoc.who.int/hq/2002/WHO_EDM_QSM_2002.2.pdf

Spontaneous Reporting in Product Quality Monitoring

Spontaneous reporting is a routine and cost-effective way of monitoring product quality problems at the national level. A notification form has been developed to allow institutions and health care professionals to alert the Regulatory Authority of problems encountered with the medicines supplied to or used by them. This important information help the safety monitoring of medicines and, in addition to notifying NPMIC, the information goes to other departments in the regulatory authority such as the registration department, inspection department, and the quality control (laboratory analysis) department. The form has been designed to incorporate the most common pharmaceutical problems encountered.

In Rwanda, even though the submission of spontaneous reporting shall be voluntarily done by healthcare professionals, they are encouraged to report all adverse events brought to their attention. Moreover, it is mandatory to report any serious adverse event which caused—

- Death
- Life threatening conditions
- Disability
- Congenital anomaly
- Hospitalization
- Modification of therapy due to toxicity

The submission of spontaneous reports of suspected adverse events should be guided by the following—

- In-time reporting
  - Report any suspected adverse drug reaction as soon as it occurs

- Accuracy and completeness
  - Each notification form must accurately and legibly be filled out with all the necessary information that is available. This is very important during causality assessment. The minimum information that is required include—
    - Patient identification
    - Detailed adverse event
    - Details on the suspected pharmaceutical product,
    - Identification of the person who has completed the adverse event notification form

  In some emergency cases, reporters can also directly contact the NPMIC to inform them about any adverse event occurred to their premises. The NPMIC will then complete a notification form on their behalf. Reporters are encouraged to have complete information ready at the time they are contacted by NPMIC for more details.

- Two types of notification forms have been developed to capture reporting related to adverse event and poor quality medicines.

    - The notification form for the reporting of all adverse events in patients exposed to a medicine or device in Rwanda is attached to these guidelines (annex A [French]; annex B [English]) and will be available at health facility level. Electronic forms can also be obtained from the MoH website (http://www.moh.gov.rw).

    - The notification form for the reporting of all poor quality problems in health facilities or at patient level in Rwanda is attached to these guidelines (annex C [French]; annex D [English]) and will be available at health facility level. Electronic forms can also be obtained from the MoH website (http://www.moh.gov.rw).

- Emergency cases and lack of forms
    - As mentioned above, in some emergencies, reporters can also directly contact the NPMIC to inform them about any adverse event that occurred on their premises.

Who Should Report?

- All health professionals
- Community health workers
- Patients, patients' relatives
- Public in general

The Rwanda notification system also allows traditional medicine practitioners and the public at large to report all adverse events related to the use of any health product to the NPMIC through Pharmacovigilance subcommittees. Such health products may include complementary and alternative medicine and nutritional and dietary supplements.

Where to Report?

- To healthcare providers in health facilities
- To Pharmacovigilance subcommittee of drug and therapeutics committee in hospital
- To the NPMIC

How to Report Adverse Events

- A patient who has experienced the adverse event should report to the nearest healthcare provider.
- At health center level, the head of health center is responsible of collecting the completed adverse event notification forms and sending them to the DTC secretariat of the nearest district hospital

- At the hospital level, the healthcare providers should fill a notification form and give it to their chief of service who forwards it to the Pharmacovigilance subcommittee at their health facilities within the defined time
- The Pharmacovigilance subcommittee validates the collected forms before sending them to the NPMIC within the defined period of time
- Once the notification form is submitted and received, there shall be a delivery note from the receiver.

How to Report Poor Quality Medicine Problems

- Any patients, healthcare professionals, or anyone else who notices/suspects a poor quality medicine should report it to the nearest healthcare provider by—
  - Filling the notification form

    or
  - Reporting the poor quality by any other means than notification
- At health center level, the head of health center is responsible of collecting the filled poor quality medicine notification forms and sending them to the hospital management which will orient them to the PV subcommittee
- At the hospital level, the healthcare providers should fill a notification form and give it to their chief of service who forwards it to the Pharmacovigilance subcommittee at their health facilities within the defined time
- The PV subcommittee should validate the collected forms before sending them to the NPMIC within the defined period of time
- Once the notification form is submitted and received, there shall be a delivery note from the receiver.

What Should Be Reported?

- Report all suspected adverse events to medicines, traditional/herbal medicines, X-ray contrast media, medical devices, cosmetics, nutritional and dietary supplements, and other health products which are not mentioned here.
- In addition to the ADR, report medicine quality problems noticed at patient level such as—
  - Color change
  - Separation of components
  - Powdering/crumbling
  - Caking
  - Molding
  - Change in smell
  - Poor packaging
  - Poor labeling and mislabeling
  - Suspected contamination
  - Questionable stability
  - Defective components
  - Expired medicines

When to Report?

- Serious adverse events should be reported immediately to the NPMIC or its decentralized unit as they occur or as the reporter learns about them. When those reports are sent to the PV subcommittees, those units are requested to transmit them to the NPMIC without any delay.

- The notification form for serious adverse events must be filled within 24 hours and sent to the NPMIC within 48 hours from the time of notification.

- Serious adverse events must be reported to the head of clinical services in the health facility before being sent to the NPMIC

- Other adverse event reports should be received at NPMIC not later than one month after they have been reported to the health facility.

- Poor quality medicine should be reported as soon as possible, it follows the same scheme as the adverse events.

What Happens to a Report?

- The submitted report is validated and entered into the national database of adverse events. This database enables the NPMIC to keep track of all adverse event reports received nationwide.

    - For adverse event, the reports are routinely analyzed using the WHO and French methods as they are received and documented in a standard format for the determination of causality by the NPMIC.

    - For poor quality medicines, the reports are analyzed by a team composed by representatives of the Medicine Inspection, Medicine Registration services, NPMIC staff, Rwanda Bureau of Standards and laboratory of medicine analysis.

- The information obtained from these analyses will be submitted to the NMRA to help the MoH in decision making. NPMIC will disseminate conclusions from analysis reports and related decisions through existing communication channels.

- The NPMIC will regularly send—

    - Analyzed adverse event notifications to the UMC

    - Analyzed notifications of poor quality medicines to inspection, registration, and lab analysis department for further actions

- A well-completed and duly submitted adverse events and poor quality medicine notification form by a health professional may result in—
  - Additional investigations into the use of the medicine in Rwanda
  - Appropriate changes of the package and notice
  - Changes in the ways of using the pharmaceutical product
  - Enhancing educational initiatives to improve the safe use of that medicine
  - Other regulatory and health promotion interventions as the situation may warrant including product withdrawal/recall

How Do the Healthcare Provider and Patient Benefit from Reporting?

The healthcare provider and patient benefit from reporting through—

- Improved quality of care offered to patients
- Reduced medicine-related problems leading to a better treatment outcome
- Improved patient confidence in professional practice, hence professional growth
- Improved knowledge
- Access to feedback information on medicine-related problems reported within the country and internationally
- Satisfaction in fulfilling a moral and professional obligation

Use of Spontaneous Reporting in Medication Error and Patient Safety Monitoring

The notification form in Rwanda contains fields for the documentation of medication errors occurred simultaneously with an adverse event. The NPMIC shall monitor medication errors and assess their root causes to contribute in improving patient care. The NPMIC will use an updated version of the US National Coordinating Council for Medication Error Reporting and Prevention index for categorizing medication errors.

Protection of the Healthcare Professionals Who Report Adverse Events

- Reporting an adverse event does not necessarily mean that the healthcare professional or the medicine has contributed to or caused it.

- The outcome of the notified adverse event will be communicated to the healthcare provider who reported the case.

- The information given in the notification form is strictly confidential up to the central database level.

- The information obtained from reports will not be used for commercial purposes, but is intended to improve the rational use of pharmaceutical products.

Active Surveillance

The spontaneous reporting system remains the backbone of medicine safety monitoring in Rwanda. Active surveillance methods can be used in further validating spontaneous report signals generated through the NPMIC spontaneous notification system. However, because of the known limitations of spontaneous reporting including the lack of denominator data, lack of controls, poor case documentation, and the inability to ascertain the report's validity, the NPMIC should promote conducting relevant active surveillance studies in Rwanda. The overall responsibility for the monitoring of active surveillance studies and other pharmacoepidemiology studies remain the prerogative of NPMIC.

General Guidelines for Conducting Pharmacoepidemiological Studies

In general, local and international experts and organizations interested in conducting pharmacoepidemiology studies in Rwanda will require formal technical approval from the NPMIC in addition to the Rwanda National Ethics Committee and the NMRA approval for the study to take place. Researchers are also advised to review and, as much as possible, comply with the guidelines for good pharmacoepidemiology practices[6] and related WHO publications.[7,8] These guidelines recommend the following when conducting these studies—

- All pharmaco-epidemiology study proposals should be submitted to the NMRA which will then set research priorities and ensure that the following issues are clearly identified—
  - Study objectives
  - Active surveillance method
  - Capacity to implement method
  - NPMIC Involvement
- There should be a detailed protocol developed for the study.
- Responsibilities and plans to ensure compliance to national ethical standards should be clearly stated
- Protocol should be approved by the ethical committee.
- Research findings should be reviewed and approved before publication by the NMRA.

[6] International Society for Pharmacoepidemiology. 2008. Guidelines for Good Pharmacoepidemiology Practices, GPP. *Pharmacoepidemiology and Drug Safety* 17: 200–208.

[7] WHO. 2006. *The safety of medicines in public health programmes: Pharmacovigilance an essential tool.* Geneva: WHO. http://www.who.int/medicines/areas/quality_safety/safety_efficacy/Pharmacovigilance_B.pdf.

[8] WHO. 2007. *Pharmacovigilance for antiretrovirals in resource-poor countries.* Geneva: WHO. http://www.who.int/medicines/publications/PhV_for_antiretrovirals.pdf

Some active surveillance methods used in Rwanda

To implement plans for routine active surveillance activities, the NMRA will ensure that SOPs are in place for conducting active surveillance studies. After identifying research priorities, the authority will provide technical guidance on the preferred active surveillance method to be used. The following active surveillance methods can be used—

- Cohort event monitoring
- Case control studies
- Prescription event monitoring
- Medicine/device exposure registries
- Medicine utilization studies

The PHPs can identify their research priorities based on prevalence, frequency and importance of ADR spontaneous reports related to their specific products. They should therefore regularly collaborate with the NPMIC and identify important signals that may require validation using active surveillance methods.

SAFETY MONITORING OF HERBAL MEDICINES IN THE NATIONAL PHARMACOVIGILANCE SYSTEM

In developing countries, some herbal medicines are considered to be more readily available, accessible, affordable, culturally acceptable and sustainable than Western medicines. In developed countries, the popularity of herbal medicines continues to grow, particularly for treating certain disease categories.

However, herbal medicines are not necessarily always safe simply because they are natural. Some have given rise to serious adverse reactions and some contain chemicals that may produce long-term side effects such as carcinogenicity and hepatotoxicity. Herbal medicines will only benefit the health of human beings when they are used appropriately. Thus, good quality control and standardization of herbal medicines are essential. Furthermore, with the increased use of both herbal medicines and modern western pharmaceutical drugs, there is a need to monitor interactions.

Reporting adverse events related to herbal medicines shall be the same as for the other health products mentioned in this guideline and shall involve cooperatives made up of traditional healers that are officially approved by the appropriate authorities.

The national policy on traditional and herbal medicine as well as related guidelines shall be the referral and support documents.

TOOLS FOR MEDICINE SAFETY SURVEILLANCE ACTIVITIES

Pharmacovigilance activities involve the use of several validated tools to generate and analyze data to guide decisions. In an effort to standardize all Pharmacovigilance and medicine information system processes in Rwanda, the following tools have been developed and adopted for key activities of the NPMIC. These tools can be revised if needed.

Adverse event notification form

The Adverse Event Notification Form (annex A–French; annex B–English) is the official tool by which all suspected adverse events shall be reported. It is designed to be short, simple, and easy to complete. The notification form collects important details pertaining to the suspected adverse events. The form should be used for the following events—

- All suspected adverse events related to the use of medicines and medical devices
- All suspected adverse events related to the use of complementary and alternative medicines, traditional/herbal medicines, and cosmetics, nutritional and dietary supplements

Poor quality medicine notification form

The poor quality medicine notification form (annex C–French; annex D–English) is the official tool by which all suspected poor quality medicines shall be reported. It is designed to be short, simple and easy to complete. The notification form collects important details pertaining to the poor quality medicine. The form should be used for the following—

- Color change
- Separation of components
- Powdering/crumbling
- Caking
- Molding
- Change in smell
- Poor packaging
- Poor labeling and mislabeling
- Suspected contamination
- Questionable stability
- Defective components
- Expired medicines

Medicine information request form

The medicine information request form (annex E) is the official tool in Rwanda for making requests to the NPMIC for information related to medicines or health products and related pharmacotherapy issues. The scope of what can be included in a request for medicine information is—

- Mode of administration and dosage
- Indication and choice of therapy
- Interactions (drug-drug, drug-disease, etc.)
- Adverse effects and toxicities
- Management of poisoning
- Product identification, packaging, labeling
- Product manufacturer and availability
- Medicine utilization data
- Disease profile and management
- Recent evidence and studies on specific diseases and medicines
- Epidemiology of diseases in Rwanda
- Any other related questions

Requesting for medicine information can also be through phone calls and e-mail messages. Clients are requested to clearly specify what information they seek so that they can receive answers that precisely answer their questions. The NPMIC has developed standard tool for providing responses to the enquirer.

Causality assessment tool

After adverse event reports are received, the NPMIC works closely with the NMSC to determine causality between the reported event and the health products the patient or consumer has been exposed to. There are several scales for determination of causality. In Rwanda, the NPMIC uses the WHO causality assessment criteria as the official reference for deciding on the contribution of the health product to the adverse event. The criteria are classified as Certain, Probable/Likely, Possible, Unlikely, inaccessible/unclassified and conditional/unclassified. The WHO causality assessment criteria tool is attached as annex F.

Adverse event severity grading scale

When adverse events are reported in Rwanda, the severity of the event will be determined through an evaluation of the report, medical records and further discussions with the reporter. Understanding of the severity of adverse events will guide the decisions about adverse events that are of importance for further studies in Rwanda. It will also provide information for the education of healthcare workers on adverse events and their management. In Rwanda, the WHO toxicity grading scale for determining the severity of adverse events will be the official reference for the grading of severity of adverse events. The tool is attached as annex G.

Medication error assessment tool

When medication errors are identified and reported, there are opportunities for learning from the experience and preventing further errors. The NPMIC provides advocacy and resources for the monitoring and learning from medication errors and patient safety problems. In Rwanda, the American National Coordinating Council for Medication Error Reporting and Prevention Index, (NCC MERP) will be the reference for grading medication errors in Rwanda. The NCC MERP index is attached as annex H.

Patient Alert Card

The Patient Alert Card notifies all healthcare providers that its bearer has experienced some serious intolerance (typically hypersensitivity reactions) to a particular medicine. This will help them to identify the patient's medicine-related intolerence and prevent the same (or similar) medicine reactions. The card is expected to be carried by the patient all the time and must be presented to healthcare providers during consultation or dispensing time . The Patient Alert Card for official use in Rwanda is attached as annex I (annex J is Patient Alert Card in Kinyarwanda). This card will be delivered by the DTC/PV subcommittee and inform the NPMICfor registration.

Glossary of medicine safety terms

To ensure common understanding of all terms used in medicine safety surveillance activities in Rwanda, standard official definitions as applicable to Rwanda have been provided for relevant Pharmacovigilance and medicine safety terminologies. Users are encouraged to review these terms and use them in the same definition and meaning as it has been provided in this document. The official glossary of medicine safety terms are provided as annex K.

All health care workers are encouraged to use these tools as indicated and continuously provide positive criticisms on their improvement to the NPMIC. The NPMIC, in consultation with various stakeholders, will review these guidelines and tools periodically, to ensure that they continue to meet the goals of Pharmacovigilance and medicine information activities in Rwanda.

CAPACITY BUILDING

Staff members working at health facilities require continuous capacity building activities on Pharmacovigilance. ADRs are not well understood and, in many countries, are seldom detected. Attention to monitoring also may be neglected, and thus staff members need to stay aware that ADR monitoring is part of their good clinical practices. Trainings are required to ensure that staff members understand prescribing practices for new medicines, the correct dosage regimen and how treatment failures are managed. Staff members also need to be taught how to detect ADRs, where to refer the patients and how to complete the ADR reporting form accurately. In addition, continuous clinical guidance for improved recognition of adverse reactions is required. Staff will need to feel confident and motivated in reporting while assisting the NPMIC in its mission. Common concerns and barriers to reporting by healthcare personnel will be addressed in such capacity building activities.

The MoH, through technical assistance of SPS, has developed the National Curriculum and Training Module for Pharmacovigilance. The purpose of this training is to equip all healthcare workers across the healthcare delivery system with the necessary skills, knowledge, and attitudes that will enable them to effectively identify, assess, and report ADRs; and take appropriate action to improve medicine safety. The trainings started with a training of trainers limited to a small number of healthcare providers, essentially doctors and pharmacists, who will be subsequently called upon to conduct the national training for selected DTC members at the hospital level. With the support of training of trainers' core group, NPMIC supervised service trainings throughout the country at district level, using the trained DTC members as trainers in their respective health facilities.

The NPMIC routinely coordinates any other capacity building activities at national and hospital level to ensure the correctness and relevance of the delivered information while avoiding unnecessary dispersion of efforts. On the other hand, in order to enable NPMIC and NMSC to conduct causality assessment and analysis, there is a need to deeply capacitate the respective members on different pharmaco-epidemiologic methods.

MONITORING AND EVALUATION

For effective Pharmacovigilance and medicine information activities in Rwanda, the NMRA shall identify some performance measures for monitoring Pharmacovigilance activities of both NPMIC and the PHPs. These performance measures include indicators, reports and performance targets that will be routinely reported to the NMRA.

ANNEXES

ANNEX A. ADVERSE EVENT NOTIFICATION FORM

A.1. FRENCH VERSION:
FICHE DE NOTIFICATION DES EVENEMENTS INDESIRABLES

REPUBLIQUE DU RWANDA

MINISTERE DE LA SANTE

Centre National de Pharmacovigilance
Et d'Information Pharmaceutique

FICHE DE NOTIFICATION DES EVENEMENTS INDESIRABLES

A. Informations sur le patient

Adresse du patient	Village :		Secteur		
	Cellule :		District		
Autres adresses disponibles (téléphone/email)					
N° d'identification du patient (N° fiche, consultation, etc.)	Date naissance ...……/..……/..…… ou Age ……		Poids (Kg)	Taille (en cm)	Sexe ☐ F ☐ M
Grossesse ? ☐ Oui ☐ Non ☐ Pas Connu	Si oui, âge gestationnel (en Semaine d'aménorrhée):		La femme enceinte est : ☐ Primipare ☐ Multipare		
Le patient a-t-il une (des) maladie(s) chronique(s) ? ☐ Oui ☐ Non ☐ Pas connu Si Oui, lesquelles (compléter si nécessaire)			1		
2	3		4		
Facteurs de risque associés (encerclez): tabac, alcool, l'histoire clinique du patient, antécédent familial, les allergies, …). Décrivez les autres facteurs associés s'il y en a (*ajouter une feuille supplémentaire si nécessaire*):					

B. Informations sur les événements indésirables qui pourraient être dus au produit de santé

Description de l'événement indésirable :				
Date et heure de début de réaction ….. /…../….. à …..h……	Délai d'apparition de la réaction (en heures/jours): ……		Date et heure d'arrêt de réaction si applicable …../…../….. à …..h……	
Information sur le produit de santé suspecté				
Nom générique du produit ou nom vernaculaire, forme et dosage :		Nom de la spécialité/fabricant :		
Date de fabrication :	Date d'expiration :		No de Lot/batch N° :	
Le produit est il prescrit ? ☐ Oui ☐ Non	Pour quelle raison le produit a-t-il été prescrit (indication) :			
Dose Prescrite :	Fréquence prescrite :		Durée du traitement	
Dose prise :	Fréquence de prise par jour :			
Date/si possible heure de début de prise du produit :		Date/ si possible heure d'arrêt de prise du produit :		
Voie d'administration utilisée par le patient :		Détails sur la dilution (si applicable) :		
Où est-ce que le patient s'est-il procuré le produit ?				
Est-ce la première fois que le produit suspecté est pris ? ☐ Oui ☐ Non. Si Non, l'effet était-il apparu auparavant ☐ Oui ☐ Non				
Y a-t-il eu des mesures prises pour gérer/traiter l'événement indésirable ? ☐ Oui ☐ Non				
Si oui, spécifier les moyens utilisés pour gérer l'effet indésirable observé (traitement médicamenteux, référence, arrêt du traitement, conseils, changement de traitement,…)				
Evolution de l'événement indésirable				
☐Guérison sans séquelles ☐Pas encore guéri	☐Hospitalisation ☐ Prolongation d'hospitalisation	☐ Mise en jeu du pronostic vital ☐ Incapacité permanente	☐ Décès ☐ Pas connu	☐ autre : spécifier

C. Autres produits utilisés Y a-t-il d'autres produits utilisés par le patient ? ☐ Oui ☐ Non. Si oui compléter le tableau ci-dessous (*Ajouter une feuille supplémentaire si nécessaire*)

	1	2	3
Nom du produit			
Indication			
Posologie utilisée par le patient			
Voie d'administration telle que utilisée par le patient			
Date (et si possible heure) de début			
Date (et si possible heure) d'arrêt			

D. Informations sur le notificateur

Nom et Prénom *	
Qualification * :	Lieu de travail /FOSA*
Adresse postale* :	Téléphone du lieu de travail/FOSA *
Email :	Date*

Votre appui au système de Pharmacovigilance est grandement apprécié.

La soumission d'une plainte n'implique en aucun cas que le médicament ou le prestataire des soins ont causé ou contribué à l'apparition de cet événement. Toute information est strictement confidentielle et le personnel du système de Pharmacovigilance ne mettra jamais en public l'identité du rapporteur/notificateur en réponse à une quelconque demande publique. L'information que vous fournissez contribuera à l'amélioration de la qualité des soins et la sécurité d'utilisation du médicament.
Une fois remplie, veuillez envoyer cette fiche **au Centre National de Pharmacovigilance (CNPIP) ou au sous comité de Pharmacovigilance de l'hôpital qui vous est proche.**

Que peut vous apporter le CNPIP ?

Le CNPIP est au service de tous les professionnels de santé tant du secteur public que privé pour :

- Recueillir et analyser toute suspicion suggérant un effet indésirable dû à un produit de santé afin d'établir la relation de cause à effet
- Répondre aux questions relatives à l'utilisation des produits de santé
- Evaluer les risques d'une exposition aux produits de santé chez les personnes à haut risque
- Diffuser les informations sur la Pharmacovigilance aux professionnels de santé, aux patients/consommateurs et au grand public

Notification des effets indésirables au CNPIP

La Pharmacovigilance a pour objet la détection, l'évaluation et la prévention des effets indésirables de tout produit de santé survenant dans une population.

Les produits de santé concernés par cette notification sont :

- Les produits pharmaceutiques
- Le sang et ses dérivés
- Autres produits de santé notamment les produits alimentaires et cosmétiques, ainsi que les produits biologiques tels que les cellules humaines, les tissus, et les produits à base de cellules ou de tissus.

Qui doit notifier?

- Tous les professionnels de santé

Que faut-il notifier ?

- Tout événement indésirable, clinique ou biologique, observé chez un patient et coïncidant avec l'exposition à un produit de santé, connu ou non connu, grave ou bénin.

Comment notifier ?

- La notification du cas doit se faire sur cette « fiche de notification des effets indésirables » du Ministère de la Santé.
- La notification du cas peut se faire par :
  - Courrier : BP 84 Kigali
  - E-mail : rwandapvcenter@moh.gov.rw
    rwandapvcenter@gmail.com
  - Site web : www.moh.gov.rw

Veuillez noter que :

- La notification du cas se fait même si vous n'êtes pas sûrs que ce soit le produit suspecté qui est à la base de l'effet indésirable ou quand vous n'avez pas suffisamment de données.
- La soumission d'une fiche de notification n'implique pas automatiquement que le professionnel de santé ou le produit a causé ou contribué à l'apparition de l'effet indésirable.
- La fiche de notification remplie doit être acheminée vers le niveau supérieur endéans 48 heures
- Toutes les informations rapportées sur cette Fiche sont **strictement confidentielles**.
- Les informations sur le notificateur qui sont accompagnées du signe * sont obligatoires.
- Pour les sites ART, le dispensateur des soins identifiera le patient par son code TRACNET.

REPUBLIC OF RWANDA

MINISTRY OF HEALTH

A.2. ENGLISH VERSION: ADVERSE EVENT NOTIFICATION FORM

National Pharmacovigilance and Medicine Information Center

ADVERSE EVENT NOTIFICATION FORM

A. Patient Information

Patient address	Village :		Sector:	
	Cell :		District:	
Other available address (cell phone/email,…)				
No of patient file/dossier	Date of birth ...……/..……/..…… or age ……	weight (Kg)	height(cm)	Sex ☐ F ☐ M
Pregnancy? ☐ Yes ☐ No ☐ Don't know	If yes, indicate the length of pregnancy in weeks (amenorrhea weeks):	The pregnant woman is : ☐ primiparous ☐ multiparous		
Does the patient have any chronic diseases? ☐ yes ☐ No ☐ don't know If yes, list those diseases (diabetes, tuberculosis) in the following areas (you can add another paper if needed)		1		
2	3	4		
Associated risk factors (tick on the following ones): tobacco use, alcohol use, clinical background, familial history, allergies … Describe any other risk factors if applicable (you can add another paper on this if needed):				

B. Information on adverse events related to suspected health product

Description of the adverse event :				
Date and time of when adverse reaction started ….. /…../….. at ……h…… min	Time to onset of reaction (hours/days): ……	Date and time when reaction stopped …../…../….. at …..h……min		
INFORMATION ON THE SUSPECTED HEALTH PRODUCT				
Name of the product in INN or local name (if plant medicine), form and dosage :	Brand name/manufacture :			
Manufacture date :	Expiry date :	Batch No :		
The product was prescribed? ☐yes ☐ No	If the product was prescribed, indicate the reason why :			
Dosage Prescribed :	Frequency of daily dosing prescribed :	Treatment duration :		
Dosage taken :	Frequency of daily dosing use by patient:			
Date, if possible time of the starting taking the suspected product:	Date, if possible, the time the suspected product was stopped:			
The administration route used by patient :	Details on the dilution (if applicable) :			
Where patient got this product from?				
Is it the first time the patient has taken the suspected product? ☐ yes ☐ No. If no, did he experiment the same reactions the last time he/she took this product? ☐ yes ☐ No				
Is there any measure taken to manage /treat this adverse event? ☐ yes ☐ No				
If yes, indicate these measures (pharmaco-therapy, refer the patient, stop the treatment, change the treatment, etc….)				
Evolution of adverse event				
☐ Recovery without sequelae ☐Not recovered yet	☐Hospitalization ☐ Prolonged hospitalization	☐ Life threatening ☐ Permanent incapacity	☐ Deceased ☐ Unknown	☐ others : specify

C. Other products used: Is there any other product used by patient? ☐ Yes ☐ No. If yes, fill the table below (*Add a new page if needed*)

	1	2	3
Name of the Product			
Indication			
Dosage used by patient			
Administration route used by patient			
Date (time if applicable) of start to take the product			
Date (time if applicable) of stop to take the product			

D. Information on the notificator

Name *	
Qualification * :	Place of Work/Health Facility*
PO box* :	Phone number/yours or for the Health Facility*
Email :	Date*

Your support in this Pharmacovigilance program is appreciated.

Submission of a complaint does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event. All information is held in strict confidence and programme staff is not expected to and will not disclose reporter/notificator's identity in response to any public request. Information supplied by you will contribute to the improvement of medicine safety and therapy in Rwanda.
Once completed **please send to: National Pharmacovigilance and Medicine Information Center (NPMIC) or to the Drug and Therapeutic Committee (DTC) of the nearest hospital.**

ANNEX B. POOR QUALITY MEDICINE NOTIFICATION FORM

B.1. FRENCH VERSION:
FICHE DE NOTIFICATION SUR LA QUALITE DES MEDICAMENTS

REPUBLIQUE DU RWANDA

MINISTERE DE LA SANTE

CENTRE NATIONAL DE PHARMACOVIGILANCE ET D'INFORMATION PHARMACEUTIQUE

FICHE DE NOTIFICATION SUR LA QUALITE DES MEDICAMENTS

A. Informations sur le rapporteur

Veuillez cochez la case suivante selon votre statue	1. patient ☐ 2. Professionnel de la santé ☐ 3. autres : spécifier : ☐	Date de la notification : ……J/……..M/……A
Adresse du rapporteur — Village :	Secteur	
Cellule :	District	
Autres adresses disponibles (téléphone/email, lieux de travail, etc…)		
Le rapporteur a-t-il pris le médicament	☐ Oui ☐ Non	

B. Identification du produit

Nom de spécialité			Nom générique		
Numéro de lot		Date de fabrication		Date de péremption	
Date d'acquisition/achat		Nom du producteur et son pays d'origine			
Nom du fournisseur (hôpital, pharmacie, etc..)			Adresse du distributeur		

FORMULATION DU PRODUIT (cocher le cas échéant)	**PLAINTES A L'ENCONTRE DU PRODUIT** (cochez le cas échéant)
☐ Comprimé Oral/Capsule ☐ Suspension buvable ☐ Sirop ☐ Injection ☐ Poudre pour reconstitution d'une suspension ☐ Poudre pour reconstitution d'une injection ☐ Gouttes nasales ☐ Gouttes Oculaires ☐ Solution nébuliseur ☐ Crème/ gel/pommade ☐ Autres :……	☐ Changement de couleur ☐ Agglomération/ grumeaux ☐ Visqueux (formes solides) ☐ Changement d'odeur ☐ Séparation des composants ☐ Effritement ☐ Mauvais étiquetage ☐ Conditionnement incomplet ☐ Autres : …… ……
Décrivez en détails votre plainte …… ……	

C. Condition de stockage

Le produit requiert-il une réfrigération ?	☐ Oui	☐ Non	Autres : détailler
Le produit est-il disponible à la Formation Sanitaire ?	☐ Oui	☐ Non	
Le produit est-il retourné par le patient après qu'il ait été dispensé	☐ Oui	☐ Non	
La conservation/stockage du produit est-elle conforme aux directives du producteur ou du MINISANTE	☐ Oui	☐ Non	

D. Circonstances et moment de détection du problème de qualité du produit

A quel moment avez-vous constaté que le médicament avait un problème de qualité ?	Dans quelle circonstance avez-vous constaté ce problème de qualité
☐ Avant la prise du médicament ☐ Au cours de la prise du médicament ☐ A la fin de la prise du médicament ☐ Quand un proche (parent ou ami/e) a pris ce médicament ☐ Quand un patient que vous traitez/suivez a pris ce médicament ☐ Autres : spécifiez……	☐ A la suite d'une complication de l'état d'un patient/ami(e)/parent après la prise du médicament ☐ A la suite d'une hospitalisation du patient après la prise du médicament ☐ A la suite d'une plainte du patient ☐ A la suite d'un constat personnel dans le lieu de stockage du médicament
Si vous ou quelqu'un d'autre aviez déjà pris ce médicament, avez-vous constaté des symptômes/signes cliniques suspects ? Oui ☐ Non ☐ Si oui veuillez remplir la fiche de notification des événements indésirables.	

Votre appui au système de Pharmacovigilance est grandement apprécié.

La soumission d'une plainte n'implique en aucun cas que le médicament ou le prestataire des soins ont causé ou contribué à l'apparition de cet événement. Toute information est strictement confidentielle et le personnel du système de Pharmacovigilance ne mettra jamais en public l'identité du rapporteur/notificateur en réponse à une quelconque demande publique.

L'information que vous fournissez contribuera à l'amélioration de la qualité des soins et la sécurité d'utilisation du médicament.
Une fois remplie, veuillez envoyer cette fiche au Centre National de Pharmacovigilance ou au sous comité de Pharmacovigilance dans l'hôpital qui vous est proche.

B.2. ENGLISH VERSION: POOR QUALITY MEDICINE NOTIFICATION FORM

REPUBLIC OF RWANDA

MINISTRY OF HEALTH

National Pharmacovigilance and Medicine Information Center

Poor Quality Medicine Notification Form

A. Information on the notificator

Please tick your status		1. Patient 2. Healthcare professional 3. Other (specify)	Date of notification: ……..D/……..M/……Y
Address of notificator	Village :	Sector	
	Cell :	District	
Any other available address (cell phone/email):			
Has the person who made the notification come in direct contact with the reported product?	☐ Yes ☐ No		

B. Product identity

Brand Name			Generic name		
Batch/ lot number		Date of manufacture		Date of expiry	
Date of receipt		Name of manufacturer			
Name of distributor/supplier			Distributor/supplier's address		

PRODUCT FORMULATION (tick appropriate box)	**COMPLAINT** (tick appropriate box/boxes)
☐ Oral tablet/capsule ☐ Oral suspension/syrup ☐ Injection ☐ Diluent ☐ Powder for reconstitution of suspension ☐ Powder for reconstitution of injection ☐ Eye drops ☐ Ear drops ☐ Nebuliser solution ☐ Cream/ointment/liniment/paste ☐ Other :……	☐ Colour change ☐ Separating ☐ Powdering/crumbling ☐ Caking ☐ Moulding ☐ Change of odour ☐ Mislabelling ☐ Incomplete pack ☐ Other: …… ……
Describe complaint in detail …… …… ……..	

C. Storage conditions

Does the product require refrigeration?	☐ Yes	☐ No	Other details(if necessary):
Was the product available at facility?	☐ Yes	☐ No	
Was product dispensed and returned by client?	☐ Yes	☐ No	
Was the product stored according to manufacturer/MoH recommendations	☐ Yes	☐ No	

D. Circumstance and time of poor quality detection

At which time did you notice that the poor quality problem?	In which circumstances did you notice the poor quality problem?
☐ Before taking the product ☐ While I took the product ☐ After I took the product ☐ When relatives took the product ☐ When my patient took this product ☐ Other……	☐ When I noticed complication on my patient/relative after he/she took this product ☐ When a patient was hospitalized after taking this product ☐ After a complaint of patient who is under this medication ☐ After personal observation/experience of the medicine's poor quality in the storage room

Have you experienced any adverse event or did you receive any complaint after taking this medicine?

Yes ☐ No ☐

If you, or any other person has already taken this medicine and experienced any health problem, please complete the adverse event notification form.

Your support in this Pharmacovigilance program is appreciated.

Submission of a complaint does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the event. All information is held in strict confidence and programme staff is not expected to and will not disclose reporter/notificator's identity in response to any public request. Information supplied by you will contribute to the improvement of medicine safety and therapy in Rwanda.
Once completed **please send to: National Pharmacovigilance and Medicine Information Center (NPMIC) or to the Drug and Therapeutic Committee (DTC) of the nearest hospital.**

ANNEX C. MEDICINE INFORMATION REQUEST FORM

Date:	Time Received: _____
Received by:	
Name of Requester:	
Requester Identity:	☐ Patient ☐ Pharmacist ☐ Physician ☐ Nurse ☐ Other (specify) _____
Preferred method of delivery:	☐ Phone ☐ Fax ☐ Email ☐ Mail
References required:	☐ YES ☐ NO
Contact information	Phone number: Fax number: Email address: Mailing address:
Response needed/given in:	☐ Instantly ☐ 10 min ☐ 30-60 min ☐ End of day ☐ When time permits
Summary of the question	
Pertinent Background Information (if possible, provide more details on the chosen information)	☐ Known allergy : ..... ☐ Chronic illnesses: ..... ☐ Pregnancy: ..... ☐ Breastfeeding: ..... ☐ Concurrent medications :..... ..... ☐ Others:.....
Type of Request:	☐ Indication/choice of therapy ☐ Therapeutics Alternatives ☐ Dosage ☐ Mode of Administration ☐ Mode of action ☐ Toxicity ☐ Contra-indications ☐ Precautions to be taken while on treatment ☐ Adverse Drug Reaction ☐ Interactions (Drug-drug/drug-disease/drug-food) ☐ Medicine Identification/Packaging/labelling ☐ Product availability ☐ Other (specify)
Search Strategy:	☐ Consultation of other colleagues ☐ Consultation of specialists ☐ Documentation in a book/article/journal ☐ Internet documentation ☐ Others (please specify) _____
Response given :	
References:	

ANNEX D. WHO CAUSALITY ASSESSMENT CRITERIA

Causality assessment criteria[1]

1. *Certain:*

- Clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration, and which
- Cannot be explained by concurrent disease or other drugs or chemicals.
- Response to withdrawal of the drug (dechallenge) should be clinically plausible.
- Event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary.

2. *Probable/Likely:*

- Clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug
- Unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal (dechallenge)
- Rechallenge information is not required to fulfill this definition.

3. *Possible:*

- Clinical event, including laboratory test abnormality, with a reasonable time sequence to administrations of the drug, but which
- Could also be explained by concurrent disease or other drugs or chemicals
- Information on drug withdrawal may be lacking or unclear.

4. *Unlikely:*

- Clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which
- Other drugs, chemicals or underlying disease provide plausible explanations.

5. *Conditional/Unclassified:*

- Clinical event, including laboratory test abnormality, reported as an adverse reaction, about which
- More data is essential for a proper assessment, or the additional data is under examination.

6. *Unassessable/Unclassifiable:*

- Report suggesting an adverse reaction which
- Cannot be judged because information is insufficient or contradictory, and which
- Cannot be supplemented or verified.

[1] WHO Causality categories in WHO (2000) Safety Monitoring of Medicinal Products: Guidelines for setting up and running a Pharmacovigilance Center. *the* Uppsala Monitoring Centre (*the* UMC), WHO Collaborating Centre for International Drug Monitoring. ISBN 91-630-9004-X

ANNEX E. WHO TOXICITY GRADING SCALE

Appendix: WHO TOXICITY GRADING SCALE FOR DETERMINING THE SEVERITY OF ADVERSE EVENTS

CHEMISTRIES (continued)				
Hyperglycemia (note if fasting)	116 - 160 mg/dL	161- 250 mg/dL	251 - 500 mg/dL	> 500 mg/dL or ketoacidosis or seizures
Hypocalcemia (corrected for albumin)	8.4 - 7.8 mg/dL	7.7 - 7.0 mg/dL	6.9 - 6.1 mg/dL	< 6.1 mg/dL or life threatening arrhythmia or tetany
Hypercalcemia (correct for albumin)	10.6 - 11.5 mg/dL	11.6 - 12.5 mg/dL	12.6 - 13.5 mg/dL	> 13.5 mg/dL life-threatening arrhythmia
Hypomagnesemia	1.4 - 1.2 mEq/L	1.1 - 0.9 mEq/L	0.8 - 0.6 mEq/L	< 0.6 mEq/L or life-threatening arrhythmia
Hypophosphatemia	2.0 - 2.4 mg/dL	1.5 -1.9 mg/dL or replacement Rx required	1.0 -1.4 mg/dL intensive Rx or hospitalization required	< 1.0 mg/dL or life-threatening arrhythmia
Hyperbilirubinemia	1.1 - 1.5 x ULN	1.6 - 2.5 x ULN	2.6 - 5 x ULN	> 5 x ULN
BUN	1.25 - 2.5 x ULN	2.6 - 5 x ULN	5.1 - 10 x ULN	> 10 x ULN
Creatinine	1.1 x 1.5 x ULN	1.6 - 3.0 x ULN	3.1 - 6 x ULN	> 6 x ULN or required dialysis
URINALYSIS				
Proteinuria	1+ or < 0.3% or <3g/L or 200 mg - 1 gm loss/day	2 -3 + or 0.3 - 1.0% or 3-10 g/L 1- 2 gm loss/day	4+ or > 1.0% or > 10 g/L 2-3.5 gm loss/day	nephrotic syndrome or > 3.5 gm loss/day
Hematuria	microscopic only	gross, no clots	gross+ clots	obstructive or required transfusion
CARDIAC DYSFUNCTION				
Cardiac Rhythm		asymptomatic, transient signs, no Rx required	recurrent/persistent; No Rx required	requires treatment
Hypertension	transient inc. > 20 mm; no Rx	recurrent, chronic, > 20 mm, Rx required	requires acute Rx; No hospitalization	requires hospitalization
Hypotension	transient orthostatic hypotension, No Rx	symptoms correctable with oral fluids Rx	requires IV fluids; no hospitalization required	requires hospitalization
Pericarditis	minimal effusion	mild/moderate asymptomatic effusion, no Rx	symptomatic effusion; pain; EKG changes	tamponade; pericardiocentesis or surgery required
Hemorrhage, Blood Loss	microscopic/occult	mild, no transfusion	gross blood loss; 1-2 units transfused	massive blood loss; > 3 units transfused

Section VIII: Appendices 133 February 6, 2003
Monitoring and Reporting Adverse Events

Appendix: WHO TOXICITY GRADING SCALE FOR DETERMINING THE SEVERITY OF ADVERSE EVENTS

RESPIRATORY				
Cough	transient- no Rx	treatment associated cough local Rx	uncontrolled	
Bronchospasm, Acute	transient; no Rx < 80% - 70% FEV_1 (or peak flow)	requires Rx normalizes with bronchodilator; FEV_1 50% - 70% (or peak Flow)	no normalization with bronchodilator; FEV_1 25% - 50% (or peak flow retractions)	cyanosis: FEV_1 < 25% (or peak flow) or intubated
GASTROINTESTINAL				
Stomatitis	mild discomfort; no limits on activity	some limits on eating/drinking	eating/talking very limited	requires IV fluids
Nausea	mild discomfort; maintains reasonable intake	moderate discomfort; intake decreased significantly; some activity limited	severe discomfort; no significant intake; activities limited	minimal fluid intake
Vomiting	transient emesis	occasional/moderate vomiting	orthostatic hypotension or IV fluids required	hypotensive shock or hospitalization required for IV fluid therapy
Constipation	mild	moderate	severe	distensions w/vomiting
Diarrhea	transient 3-4 loose stools/day	5-7 loose stools/day	orthostatic hypotension or > 7 loose stools/day or required IV fluids	hypotensive shock or hospitalization for IV fluid therapy required
NEURO & NEUROMUSCULAR				
Neuro-Cerebellar	slight incoordination dysdiadochokinesis	intention tremor, dysmetria, slurred speech; nystagmus	locomotor ataxia	incapacitated
Mood	mild anxiety or depression	moderate anxiety or depression and therapy required	severe anxiety or depression or mania; needs assistance	acute psychosis; incapacitated, requires hospitalization
Neuro Control (ADL = activities of daily living)	mild difficulty concentrating; no Rx; mild confusion/agitation; ADL unaffected	moderate confusion/agitation some limitation of ADL; minimal Rx	severe confusion/agitation needs assistance for ADL; therapy required	toxic psychosis; hospitalization
Muscle Strength	subjective weakness no objective symptoms/ signs	mild objective signs/symptoms no decrease in function	objective weakness function limited	paralysis

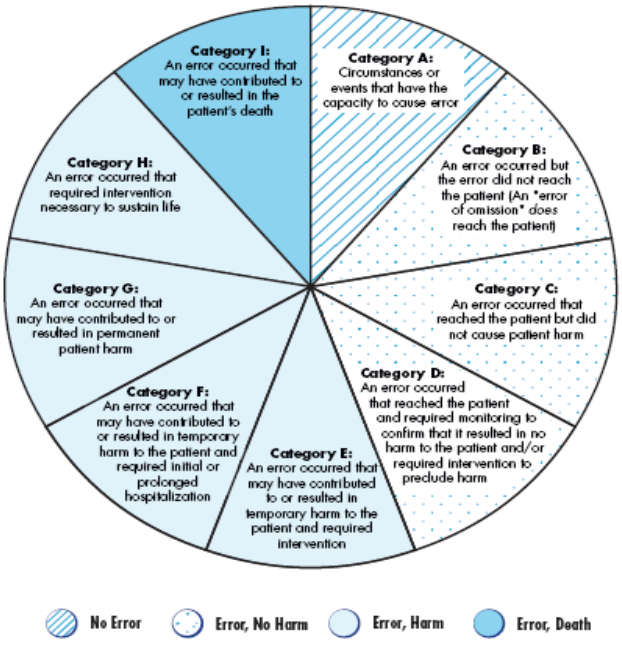
Appendix: WHO TOXICITY GRADING SCALE FOR DETERMINING THE SEVERITY OF ADVERSE EVENTS

OTHER PARAMETERS				
Fever: oral, > 12 hours	37.7 - 38.5 C or 100.0 - 101.5 F	38.6 - 39.5 C or 101.6 - 102.9 F	39.6 - 40.5 C or 103 - 105 F	> 40 C or > 105 F
Headache	mild, no Rx therapy	transient, moderate; Rx required	severe; responds to initial narcotic therapy	intractable; required repeated narcotic therapy
Fatigue	no decrease in ADL	normal activity decreased 25- 50%	normal activity decreased > 50% can't work	unable to care for self
Allergic Reaction	pruritus without rash	localized urticaria	generalized urticaria; angioedema	anaphylaxis
Local Reaction	tenderness or erythema	induration < 10 cm or phlebitis or inflammation	induration > 10 cm or ulceration	necrosis
Mucocutaneous	erythema; pruritus	diffuse, maculo papular rash, dry desquamation	vesiculation, moist desquamation, or ulceration	exfoliative dermatitis, mucous membrane involvement or erythema, multiforme or suspected Stevens-Johnson or necrosis requiring surgery

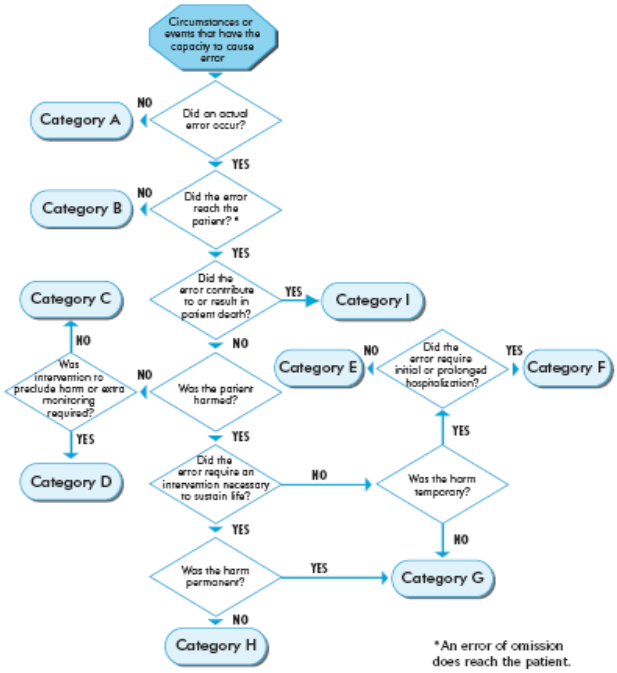
http://www.icssc.org/Documents/Resources/AEManual2003AppendicesFebruary_06_2003%20final.pdf

ANNEX F. MEDICATION ERROR REPORTING AND PREVENTION SCALE

NCC MERP Index for Categorizing Medication Errors



NCC MERP Index for Categorizing Medication Errors Algorithm



Full-size copies are available: **INDEX**—www.nccmerp.org/010612_color_index.pdf; **ALGORITHM**—www.nccmerp.org/010612_color_algo.pdf

National Coordinating Council for Medication Error Reporting and Prevention Definitions

Harm
Impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom.

Monitoring
To observe or record relevant physiological or psychological signs.

Intervention
May include change in therapy or active medical/surgical treatment.

Intervention Necessary to Sustain Life
Includes cardiovascular and respiratory support (e.g., CPR, defibrillation, intubation, etc.)

ANNEX G. PATIENT ALERT CARD

G.1. ENGLISH VERSION: PATIENT ALERT CARD

REPUBLIC OF RWANDA

MINISTRY OF HEALTH

PATIENT ALERT CARD

Patient name: ……
Date of birth: …… Gender : M ☐ F ☐ Height/Weight: …… ID/passport number: ……..
Place of issue of the alert card: PV subcommittee of Hospital…….
Date when the card was issued: ...../……./……
Responsible medicine: …….
Types of intolerance: ……..……..…… ……

Please hold always this card with you to be presented to any healthcare provider in any consultation session.

Itwaze iteka iyi karita kandi wibuke kuyereka muganga mu gihe cyose ugiye kwivuza.

Signature and stamp of the hospital

G.2. KINYARWANDA VERSION: IKARITA MPURUZA Y'UMURWAYI

REPUBULIKA Y'U RWANDA

MINISITERI Y'UBUZIMA

IKARITA MPURUZA Y'UMURWAYI

Amazina y'umurwayi……
Igihe yavukiye cyangwa imyaka: …… Igitsina : Gabo ☐ Gore ☐ Uburebure: …… Nimero y'indangamuntu/pasiporo: ……..
Aho iyi karita yandikiwe: Ibitaro bya…….
Itariki iyi karita yandikiweho: **.....**/……./……
Ubwoko bw'ingaruka mbi yatewe n'umuti: …… …….
Izina/ubwoko bw'umuti wateye icyo kibazo:……

Itwaze iteka iyi karita kandi wibuke kuyereka muganga igihe cyose ugiye kwivuza.

Kashe y'ibitaro byatangiwemo iyi karita

ANNEX H. GLOSSARY OF MEDICINE SAFETY TERMS

http://psnet.ahrq.gov/glossary.aspx

Adverse medicine reaction (AMR)/adverse drug reaction (ADR)
A response to a medicine which is noxious and unintended, and which occurs at a dose normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

The term adverse drug reaction should be considered for harmful or seriously unpleasant effects occurring at doses intended for therapeutic, prophylactic or diagnostic effect and which calls for reduction of dose or withdrawal of the drug and/or forecast hazard from future administration.

Adverse event /adverse experience
Any untoward medical occurrence that may present during treatment with a pharmaceutical products but which does not necessarily have a causal relationship with the treatment

Medication error
A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

(Source: National Coordinating Council for Medication Error Reporting and Prevention. Available from: http://www.nccmerp.org/aboutMedErrors.html)

Medicine/Drug
A pharmaceutical product, used in or on human body for the prevention (prophylaxis, mitigation diagnosis) or treatment of disease, or for the modification of physiological function

Medicine safety surveillance
The processes involved in the collection, collation, analysis and dissemination of data and other activities carried out in relations to safeguarding the safety and effectiveness of pharmaceuticals and related products

Medicine safety system
All organisations, institutions, and resources that contribute to efforts, whether in personal health care, public health services or through intersectorial initiatives, whose primary purpose is to protect the public from harm related to the use of medicines.

Periodic safety update report
A periodic safety update report is an update of the worldwide safety experience of a product obtained at defined times post registration.

Pharmacovigilance

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

Aims of Pharmacovigilance

The specific aims of Pharmacovigilance are to—

- Improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions
- Improve public health and safety in relation to the use of medicines
- Detect problems suspected to be caused by medicines and communicate the findings in a timely manner
- Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, leading to the prevention of harm and maximization of benefits;
- Encourage safe, rational and more effective (including cost-effective) use of medicines;
- Promote understanding, education and clinical training in Pharmacovigilance and its effective communication to the public.

Serious adverse event

Serious adverse event is any untoward occurrence that

1. Is life-threatening or fatal
2. Causes or prolongs hospital admission
3. Causes persistent incapacity or disability
4. Concerns misuse or dependence
5. Causes congenital anomaly/birth defect

Signal

A signal refers to "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 seriousness of the event and the quality of the information.

Side effect

Any unintended effect of a pharmaceutical products occurring at doses normally used in patients, which is related to the pharmacological properties of the medicine

Spontaneous reporting

A system whereby case reports of adverse drug events are voluntarily submitted by health professionals and pharmaceutical manufacturers to the national regulatory authority/ Pharmacovigilance centre

Toxicity

Toxicity implies cell damage from a direct action of the drug, often at a high dose, e.g., liver damage from Paracetamol overdose.

Unexpected adverse reaction

An adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from the characteristics of the drug.

ANNEX I : DEFINITION AND CLASSIFICATION OF ADR

WHO defines adverse reaction as a response to a medicine which is noxious and unintended, and which occurs at doses normally used in patients. In this prescription, it is of importance that it concerns the response of a patient in which individual factors may play an important role, and that the phenomenon is noxious.

A classification of ADRs reveals how they are related and draws attention to the common factors involved in the cause of reactions within the same group, thus enabling similar steps to be taken to treat or prevent them. Adverse drug reactions are categorized as Type A, Type B, or Type C in this method of classification.

Type A (augmented) adverse drug reactions

- These reactions are the result of an exaggerated, but otherwise normal pharmacological action of a drug given in the usual therapeutic doses.
- Type A reactions are largely predictable on the basis of a drug's known pharmacology.
- They are usually dose-dependant and although their incidence and morbidity in the community is often high, their mortality is generally low.

Type B (bizarre) adverse drug reactions

- These reactions are totally aberrant effects that are not expected from the known pharmacological actions of a drug when given in the usual therapeutic doses to a patient whose body handles the drug in a normal way.
- They are usually unpredictable and are not observed during conventional pharmacological and toxicological screening programs.
- Although their incidence and morbidity are low, their mortality may be high.

Type C adverse drug reactions

- These reactions refer to situations where the use of a drug, often for unknown reasons, increases the frequency of a "spontaneous" disease.
- They may be both serious and common and may have pronounced effects on public health.
- They may also be coincidental and may cause long-term effects. There is often no suggestive time relationship and the connection may be very difficult to prove.


RWANDA
BIOMEDICAL
CENTER
A Healthy People. A Wealthy Nation

World Health
Organization


USAID
FROM THE AMERICAN PEOPLE

USAID
President's Malaria Initia-
CDC

msh
Management Sciences for Health