GUIDELINES ON DETECTING AND REPORTING ADVERSE DRUG REACTIONS IN UGANDA

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These guidelines shall be cited as the *"Professional Guidelines on Detecting and Reporting Adverse Drug Reactions in Uganda" Doc. No. DPS/GDL/013, Revision No.:1".*

Adoption and approval of these professional guidelines

In EXERCISE of the powers conferred upon the Drug Authority by Section 5(i) of the National Drug Policy and Authority Act, Cap. 206 of the Laws of Uganda (2000 Edition), the Drug Authority hereby ADOPTS and ISSUES these Professional **Guidelines Detecting and Reporting Adverse Drug Reactions in Uganda;** Doc. No. DPS/GDL/013, Revision No.:1, made this **24th day of October 2019,** that take effect on **01st November 2019**.

Signature

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TABLE OF CONTENTS

1.0 BACKGROUND

Approval of drugs for market authorization depends on the decision that the benefit of the drug out weights its risks, based on information that accrues from pre-approval studies. The latter studies are incapable of detecting all of the investigational new products` negative effects, which may include rare but serious adverse reactions, toxicity and adverse experiences during use in special groups such as children, elderly and pregnant mothers.

As such, drugs, vaccines and surgical instruments, test kits and diagnostic devices will have the propensity to cause several previously unknown adverse reactions. It's therefore imperative that these products are vigilantly monitored post market approval to identify, remediate and communicate such negative effects as a means of enhancing patient safety and improving treatment outcomes.

"Pharmacovigilance" refers to the science and activities concerned with the knowledge, detection, assessment, understanding and prevention of adverse reactions to medicines or any drug-related problems.

A core aspect of pharmacovigilance is the voluntary reporting of AEs/ADRs by patients, physicians, nurses, pharmacists or anyone else who suspects that there may be a relationship between and AE/ADR and a drug.

This guideline is intended to assist healthcare providers, public health programs and other stakeholders, with ADE Reporting the responsibilities in meeting the requirements in the Pharmacovigilance regulations (2014).

This guideline does not apply to the Investigational new drug application safety reports.

2.0 INTERPRETATION

For the purpose of these guidelines, unless the context otherwise requires:

Act means the National Drug Policy and Authority Act; Cap 206

Adverse Drug Reaction (ADR) means "a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function.

Adverse drug reaction means a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function;

Adverse event (ADE) or experience means any untoward medical occurrence that may present during treatment with a medicine but which 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) means any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease.

Authority means the National Drug Authority;

Brand name means the name a manufacturer assigns to a product

De-challenge refers to withdrawal of a drug.

Drug means any substance or preparation used or intended to be used for internal or external application to the human or animal body either in the treatment or prevention of disease or improving physiological functions or for agricultural or industrial purposes.
Essential elements in this definition are the pharmacological nature of the effect; that the phenomenon is unintended and that there is no deliberate overdose.

Generic name means the International Nonproprietary Name (INN) established by a body of the World Health Organisation

In vitro diagnostic device means a surgical instrument that is intended to be used in vitro for the examination of specimens taken from the body of a human being or of an animal;

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 (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).

Licensed person means a person licensed under section 14 of the Act;

Life-threatening in this context refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe (ICH-E2D Guideline).

Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious, such as important medical events that might not be immediately life-threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed in the definition above. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation or development of dependency or abuse (ICH-E2D Guideline). Any suspected transmission via a medicinal product of an infectious agent is also considered a serious adverse reaction.(EMA-GVP Annex 1-Definitions)

Proprietary drug means a drug distributed for sale by retail under a brand name or other proprietary description and in a form ready for use; (FROM THE act)

Re-challenge is only justifiable when the benefit of reintroducing the drug to the patient outweighs the risk of recurrence of the reaction. In some cases the reaction may be more severe on repeated exposure.

Re-challenge refers to reintroducing the drug after withdrawal.

Resolution of suspected ADR when the drug is withdrawn is a strong, although not conclusive indication of drug-induced reaction.

Serious adverse event means an adverse reaction which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.

Side effect means any unintended effect of a pharmaceutical product occurring at doses normally used by a patient, which is related to the pharmacological properties of the drug.

Signal means Information that arises from one or multiple sources (incl. observations and experiments), which suggest a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse* or beneficial, that is judged to be of sufficient likelihood to justify verificatory action" (CIOMS-2010, Pg-14)

Surgical instrument means any instrument, apparatus, implement, machine, implant, in vitro reagent or calibrator, software, material or other similar or related article and includes an appliance, which is intended by the manufacturer to be used, alone or in combination, for human beings or animals for one or more of the specific purposes of

a) diagnosis, prevention, monitoring, treatment or alleviation of disease;

(b) diagnosis, monitoring, treatment, alleviation of or compensation for an injury;

(c) Investigation, replacement, modification, or support of the anatomy or of a physiological process;

(d) Supporting or sustaining life;

(e) Disinfection of a surgical instrument; or

(f) providing information for medical purposes by means of in vitro examination of specimens derived from the body of a human being or of an animal and which does not achieve its primary intended action in or on the body of a human being or of an animal by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means;

Test kit means an in vitro diagnostic device that consists of reagents or articles, or any combination of these and that is intended to be used to conduct a specific test.

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

Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and quality of the drug.

ABBREVIATIONS

SN	Abbreviation	Full version of the abbreviation
	DIBD	Development International Birth Date
	ADR	Adverse Drug Reaction
	WHO	World Health Organisation
	INN	International Non-Proprietary Name
	NPC	National Pharmacovigilance Center
	AEFI	Adverse Event Following Immunisation
	PV	Pharmacovigilance

3.0 OBJECTIVES OF THIS GUIDELINE

To guide healthcare workers, patients, caretakers and the general public on reporting ADEs, ADRs, side effects and AEFIs associated with human drugs and vaccines. It serves to specify what, when, how, and who submits such reports to:

a) create awareness on the burden of the ADRs, the need to report and the reporting infrastructure available in the country;

b) promote early detection of adverse drug reaction in patients;

c) improve selection and rational use of drugs by healthcare workers; and

d) reduce medicine-induced morbidity and mortality.

4.0 SCOPE

These guidelines apply to reporting of ADEs, ADRs, side effects and AEFIs associated with human drugs and vaccines by healthcare workers, public health programs and the general public.

These guidelines do not apply to drugs for

5.0 POLICY

These guidelines are drawn under the National Drug Policy and Authority (Pharmacovigilance) Regulations, 2014, Statutory instrument No.37.

1) section 3(2b) states that*: "a licensed person, doctor or health professional who is involved in handling drugs intended for human use, in public health programs and programs organised and sponsored by non-governmental organizations (c) and any other person as may be determined by the authority, shall have an appropriate mechanism of monitoring the safety of the drugs that are handled in their day to day activities";*

2) Section 6 states that: *"A health care professional shall report any serious adverse drug event that arises during the process of providing health care";*

6.0 DISTRIBUTION

NDA website;

A shared folder for all staff on NDA head office server (\\ndaserver\qms\guidelines);

A shared folder for all staff on NDA laboratory server (\\ndqsvr\qms\guidelines);

Uncontrolled copies to healthcare workers, patients, caretakers and the general public

7.0 RATIONALE FOR PHARMACOVIGILANCE

Pharmacovigilance produces detailed information of marketed products to ensure their safe use.

7.1 The major aims of Pharmacovigilance are

a) Early detection of previously unknown adverse reactions and interactions.

b) Detection of increase in known adverse drug reactions.

c) Identification of predisposing risk factors and possible mechanisms underlying adverse reaction.

d) Estimation of quantitative aspects of risk/ benefits analysis and dissemination of needed information to improve drug prescribing, use and regulation.

7.2 The ultimate goal of Pharmacovigilance is to:

a) Asses and communicate risk and benefits of drugs on the market;

b) Promote rational and safe use of medicines; and

c) Educate and inform the patients about the effects of drugs.

8.0 PHARMACOVIGILANCE SYSTEM

The Pharmacovigilance system is composed of structures, processes, resources, documentation and outcomes of pharmacovigilance activities; designed to monitor the safety of medical products and health technologies. The aim is to promote safe and effective use of the products and timely provision of safety information to ensure that consumers of medical products are protected from any harm that may arise from their use. National Medicines Regulatory Authorities, Manufacturers, Market Authorization Holders, Health facilities, Public Health Programs, Suppliers and distributors of regulated products use a Pharmacovigilance system to fulfil their legal tasks and responsibilities in relation to Pharmacovigilance.

8.1 Principles for good pharmacovigilance practices (GVP)

Stakeholders should adhere to the following principles of good pharmacovigilance practices to guide the design of all structures and processes, as well as the conduct of all tasks and responsibilities:

a) The needs of patients, healthcare professionals and the public in relation to the safety of medicines should be met

b) Upper management should provide leadership in the implementation of the quality system and motivation for all staff members in relation to the quality objectives.

c) All persons within the organisation should be involved in and support the pharmacovigilance system based on task ownership and responsibility according to their tasks and assigned responsibilities.

d) All persons involved with the entire organisation should engage in continuous quality improvement

e) Resources and tasks should be organised as structures and processes in a manner that will support the proactive, risk-proportionate, continuous and integrated conduct of pharmacovigilance.

f) All available evidence on the risk-benefit balance of medicinal products should be sought and all relevant aspects, which could affect the risk-benefit balance and the use of a product, should be considered for decision-making.

g) There should be Good cooperation between the patients, health providers, Ministry of Health and National Drug Authority.

8.2 Quality systems

The pharmacovigilance system requires robust quality control and assurance system that covers the organisational structure, responsibilities, procedures, processes and resources. This system is essential for monitoring and evaluation as well as appropriate resource management, compliance management and record management as required by the current International quality standard.

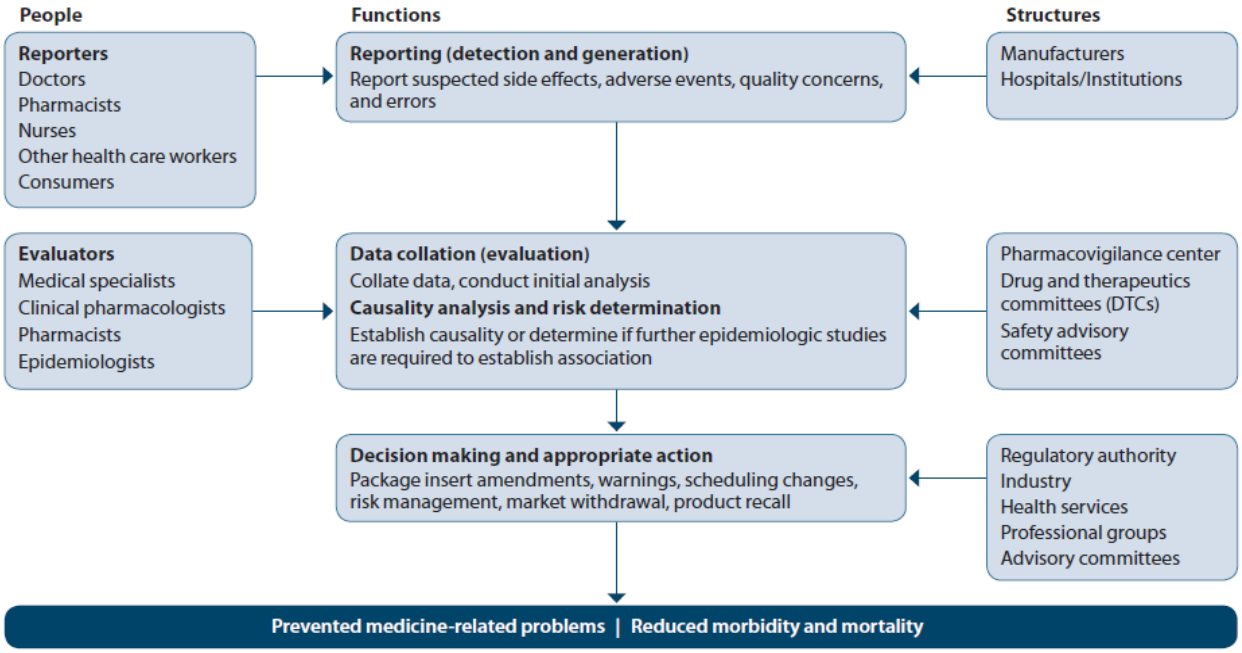
The Pharmacovigilance stakeholders shall be required to establish a quality system for all pharmacovigilance activities to produce desired outcome and quality objectives. The Pharmacovigilance quality system shall involve quality planning, adherence, control, assurance and improvements.

8.3 Quality documentation and Record management

Pharmacovigilance information should be recorded, handled and stored to allow accurate reporting, interpretation and verification. A record management system for all documents used for pharmacovigilance activities should be established to ensure that they are easily retrievable and traceable. The records shall include measures taken to investigate safety concerns, timelines taken for the investigations and the decision-making process.

Pharmacovigilance records management system shall ensure that the data is complete, accurate and of high integrity.

8.4 Flow of data in the ADR reporting process



Source: CPM/MSH 2011.

9.0 PHARMACOVIGILANCE CENTRE

The National Pharmacovigilance Centre (NPC) hosted at NDA was established to coordinate the nationwide activities of detection, remediation and communication of risk associated with potential adverse drug effects. The NPC is assisted by a National Advisory Committee comprising of experts from various fields of healthcare.

9.1 Main functions of the NPC

a. Distribute ADR report forms and collect ADR reports from Health facilities.

b) Train and sensitize Health professionals and other stakeholders on the importance of Pharmacovigilance.

c) Analyze, evaluate and maintain database of received adverse drug reactions and medicine related problems.

d) Disseminate relevant information to Health Professionals, Policy makers and other stakeholders.

e) To communicate findings to the originators of ADR reports (Feedback)

f) To participate in the WHO intervention programs on Drug Monitoring

g) Promote exchange of drug information with stakeholders within and outside the country.

9.2 Regional Pharmacovigilance Center

Regional PV Centres are established in Regional referral hospitals. These centres serve to extend the reporting infrastructure to health facilities within their catchment areas and their specific functions are delineated in specific memorandum of understanding between the centres and the NDA along with the terms of reference therein.

9.2.1 Pharmacoviglance in Public Health Programs (PHPs)

Public health Programmes (PHP) shall be actively engaged in pharmacovigilance activities and have pharmacovigilance systems as described in section 7.0 of this guideline.

The public health Programmes, as a bare minimum shall:

a) Have a focal person to coordinate pharmacovigilance activities in collaboration with NPC;
b) Include and budget for pharmacovigilance activities in their strategic plan;
c) Have a standard form for collecting ADRs
d) Collaborate with the NDA on active surveillance of specified products, develop risk management plans and follow-up patients,
e) Train and sensitise health care providers in reporting adverse drug events, quality complaints, and other drug safety concerns in the specific programs,
f) Promote rational and safe use of medicines by health care providers,
g) Educate and inform patients on the importance of reporting adverse drug events.
h) Assess and communicate risks and effectiveness of medicines used in the specific PHP in collaboration with NDA .

10.0 HOW TO REPORT

10.1 Reporting form

Reporting of ADRs, ADEs, and AEFIs should be done using the standard form shown in Appendix 3 and also available on the NDA website, public and private health facilities, and pharmacovigilance centres. This form tries to collect as much information as

possible about the suspected ADRs or medicine problems while being mindful of the health professionals or reporters time.

All the information required on the form is considered essential; therefore, complete the form to the best of your knowledge. Avoid non standard abbreviations.

10.2 Completing the ADR Reporting form (Annex 3)

The ADR form is the main method of ADR reporting. Instructions on how to complete the form are provided in Appendix 3

10.3 A valid report

For the report to be valid, it should have the following minimum information

a) Source of information

b) Patient details

c) Drug details

d) Reaction details

10.4 Alternative methods of reporting

Reporting needs to be easy and convenient and preference may vary between clinics and hospitals. Suitable methods may include:

a) **Telephone/WhatsApp line**; a reporter can call the National Drug Authority or Regional Pharmacovigilance Centre or send a WhatsApp message. The essential information, is captured or transcribed on to the suspected ADR reporting form for follow-up.

   i. Toll free line : 0800101999

   ii. WhatsApp: on 0791-415555

b) **The internet**: A web-based database (Vigiflow) is available at the regional centres.

c) Mobile application. The **Medsafe mobile app** is available for both patients and health workers to report side effects, and receive official news and alerts medicines in Uganda.

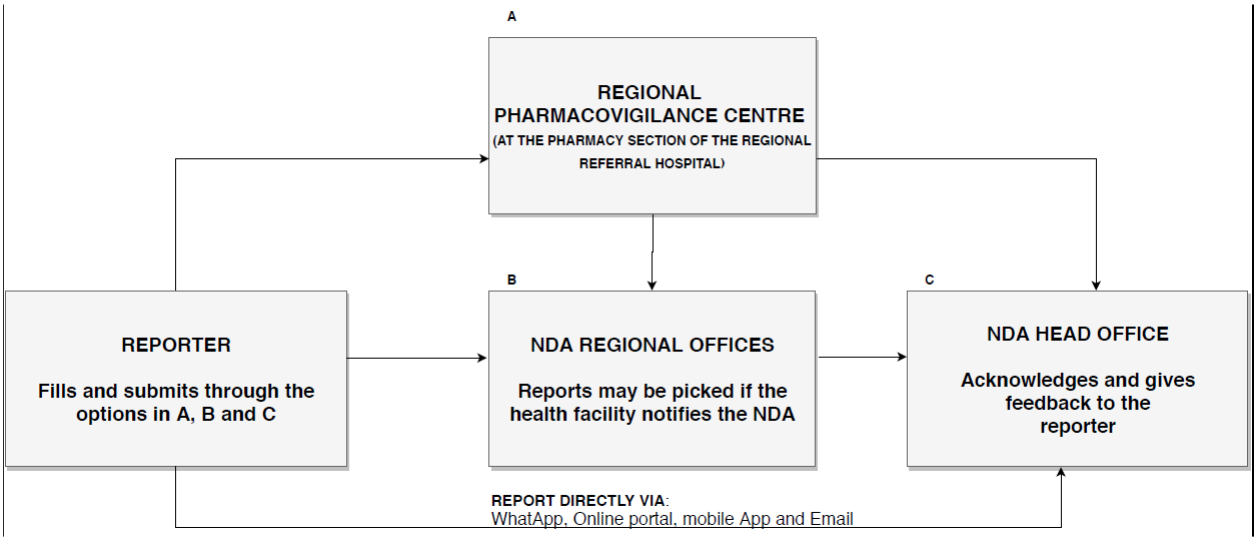
d) **An online reporting platform** available at

https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=UG

11.0 WHERE TO REPORT

Filled reports of suspected ADR should be sent to:

1: Illustration of the different routes of reporting to the National Drug Authority



a) The National Pharmacovigilance Centre at the NDA secretariat head office

b) Regional Pharmacovigilance centres in the following regional referral hospitals by hand: -

Arua Regional Referral Hospital	**Arua Regional Referral Hospital** P.O Box 03 Arua Uganda Focal contact
Gulu Regional Referral Hospital	**Gulu Regional Referral Hospital** P.O Box 160 Gulu Uganda Tel: 256(0)471432061, Fax 256(0)41250828 Focal contact
Hoima Regional Referral Hospital	**Hoima Regional Referral Hospital** P.O Box 05 Hoima Uganda Focal contact:0772664693

Jinja Regional Referral Hospital	**Jinja Regional Referral Hospital** P.O Box 43, Jinja Uganda Tel: 0772412498 Focal contact.
Kabale Regional Referral Hospital	**Kabale Regional Referral Hospital** P.O BOX 07, Kabale Uganda Tel: 0772-470297 Focal person.0772455173
Lira Regional Referral Hospital	**Lira Regional Referral Hospital** P.O Box 2,Lira Tel:+256 473 420 023/ +256 473 420 139 Focal contact:0773085939
Masaka Regional Referral Hospital	**Masaka Regional Referral Hospital** P.O Box18 Alex Ssebowa Road, Masaka Tel: 0772433809 Focol contact :0702449141
Mbale Regional Referral Hospital	**Mbale Regional Referral Hospital** P.O Box 921, Mbale, Uganda Tel: 0751519441/0773515601 Focal contact.0774123023
Mbarara Regional Referral Hospital	**Mbarara Regional Referral Hospital** P.O Box 40 Mbarara Uganda Focal contact:
Mubende regional referral hospital	**Mubende regional referral hospital** P.O Box …….. Focal contact:
Moroto Regional Referral Hospital	**Moroto Regional Referral Hospital** P.O Box 12 Moroto Uganda Tel: 0772454995 Focal contact:
Kabarole regional referral hospital	**Mubende regional referral hospital** P.O Box 40 Mbarara Uganda Focal Contact:0774483897
Mulago Regional Referral Hospital	**Mulago Regional Referral Hospital** Tel: 0772409944 Focal contact:0772947083
Soroti Regional Referral Hospital	**Soroti Regional Referral Hospital** P.O Box 289 Soroti, Uganda Tel: 0772435040/0774284949 Focal contact:0775489311

The NDA Regional Offices in:

Western Region, Hoima	Plot 29/31, main street Hoima Tel. 256 465 440688
South Eastern Region, Jinja	Plot 6 Rippon Garden, Jinja town Tel. 256 434122176
Northern Region, Lira	Plot 48. Ogwal Anjulu Road, Lira Tel. 256414671032
South Weatren Region, Mbarara	Mbaguta Estate house 29, kamukuzi 256414671034
Central Region, Nakawa (Kampala)	Premier Engeneering works ltd. Premier Plot 1-2, enterprise
Eastern Region, Tororo	Plot 27 Kwapa Road Tel. 256454445195
West Nile Region, Arua	Plot 1 Mount Wati Avenue Tel. 256414671032

Figure 2: Flow of reports from reporter to the National Pharmacovigilance Center/NDA

12.0 WHAT TO REPORT

12.1 Adverse Events, and Adverse drug reactions

Report all suspected adverse drug reactions on all drugs including herbal products and vaccines. Any ADR experienced by a patient should be reported even if you are not certain that the product caused the ADR or even if you do not have all the details.

a) For “new” drug molecules – report all suspected reactions, including minor ones. (For the purpose of this guideline, drug molecules are considered ‘new’ if the period following their marketing approval is below ten years. For example: Dolutegravir, and Bedaquiline).

b) For well-established or well-known drugs report; all serious and all unexpected (unusual) suspected adverse drug reactions.

c) Report increased frequency of any given reaction even if known (known may mean expected or previously documented).

d) Report all suspected adverse drug reactions associated with drug - drug, drug to food or drug to food supplements (including herbal and complementary products) and drug interactions.

e) Report adverse drug reactions in special fields of interest such as drug abuse and drug use in pregnancy and during lactation.

f) Report when suspected adverse drug reactions are associated with drug withdrawals.

12.2 Therapeutic failure

For all drugs (new or old) with suspected unexpected lack of efficacy should be reported. The sample (if available) should be attached to the report. Lack of efficacy may imply that either; the medicine is of poor quality, there is an interaction, there is resistance or the product is a counterfeit.

12.3 Products of questionable quality

Report product quality concerns such as:

a) Suspected contamination
b) Questionable stability
c) Defective components
d) Poor packaging or labelling
e) Expired drugs

Whenever you suspect that a product is of poor quality, report as soon as possible to the regional inspector of drugs, to NDA head office through the contacts herein or at any NDA regional offices listed herein.

12.4 Reporting suspected adverse events following the use of medical devices and diagnostics

An event/incident due to a medical device that meets the following criteria is subject to reporting to NDA:

a) A malfunction or deterioration in the characteristics or performance.
b) For IVDs (In-vitro diagnostics) where there is a risk that an erroneous result would either
    i. Lead to a patient management decision resulting in an imminent life-threatening situation to the individual being tested, or to the individual's offspring, or
    ii. Cause death or severe disability to the individual or fetus being tested, or to the individual's offspring, all false positive or false negative test results shall be considered as events. For all other IVDs, false positive or false negative results falling outside the declared performance of the test shall be considered as events.

c) Unanticipated adverse reaction or unanticipated side effect

d) Interactions with other substances or products

e) Degradation/destruction of the device (e.g. fire)

f) Inappropriate therapy

g) An inaccuracy in the labelling, instructions for use and/or promotional materials. Inaccuracies include omissions and deficiencies. Omissions do not include the absence of information that should generally be known by the intended users.

h) The medical device is considered to be the contributing cause of the incident that caused or could have caused one of the following outcomes:

a) Death of patient, user or another person.

b) A serious deterioration in state of health of a patient, user or other person in the form of:

i. life-threatening disease/illness

ii. Permanent damage, injury or impairment of a body function.

iii. Necessary medical or surgical treatment to prevent life-threatening illness, permanent injury

iv. Any indirect harm caused by incorrect diagnostic or in Vitro Diagnostic Device (IVD) test results or caused by the use of in-vitro fertilization (IVF) / assisted reproductive technology (ART) equipment used in accordance with the manufacturer's instructions for use.

v. Fatal death, fatal injury or congenital abnormalities.

Any incident, whether the fault is due to technical faults or defects in the equipment, instruction manual, marking, use or maintenance of the equipment must be reported. Events due to the intervention of healthcare professionals regardless of the serious outcome must also be reported.

On identifying a significant increase or trend of events or incidents that are usually excluded from individual reporting, the manufacturer (or license holder) must report to NDA. The manufacturer should have suitable systems in place for proactive scrutiny of trends in complaints and incidents occurring with their devices. Field Safety Notices (FSN) and Field Safety Corrective Actions (FSCA) including those based on incidents occurring outside Uganda must be reported to NDA.

The license holder may be requested by NDA to conduct a concise critical analysis of the safety and performance of the medical device or IVD and submit results within a specified time-frame. In addition, anybody can report incidents; however, healthcare professionals and manufacturers as well as MAHs, distributors and importers of medical devices are obliged to report incidents. Moreover, manufacturers must report field safety corrective actions for marketed products.

The periodic summary reports should include the full details of vigilance issues, including the status of any Field Safety Corrective Actions or Notices. All adverse events related to medical devices should be reported to NDA using the suspected adverse event/incidence reaction reporting form (Annex 3).

12.5 Recognizing ADR/ADE

Adverse Drug Reactions are difficult and sometimes impossible to distinguish from the disease being treated or prevented since they may act through the same physiological and pathological pathways.

The following step-wise approach may be helpful in assessing possible drug- related Adverse Drug Reactions:

a) **Take a proper history**

i. A full drug and medical history should be taken

ii. Can this adverse effect be explained by other causes? E.g., patient's underlying disease, other drugs, toxins or food etc.

iii. When other causes do not explain patient's condition, do thorough investigation

b) **Establish time relationships**

The time of start of therapy and time of onset of the suspected reaction should be logical; keeping in mind some reactions start immediately after start of medication while others take time to develop.

c) **Do a thorough physical examination with appropriate laboratory investigations**

i. Do laboratory test(s) especially if the drug is considered essential for patient care or if the laboratory results will improve management of the patient.

ii. Look out for distinctive physical signs and carefully evaluate the symptoms described by the patient

iii. Try to describe the reaction as clearly as possible and where possible, provide an accurate diagnosis.

iv. Use relevant up-to date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction.

d) **Effect of de-challenge and re-challenge should be determined**

i. Positive de-challenge means improvement/remission of the adverse event on withdrawal of the drug

ii. Re-challenge means reintroducing the drug after a de-challenge (re-challenge is not advisable as reactions have the propensity to recur with greater severity)

e) Check the known pharmacology of the medicine

i. Is the reaction known to occur with the suspected particular drug as stated by the package insert or other reference materials?

ii. Note: If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine.

iii. The National formularies, summary of product characteristics, research publications and international health bodies are very important sources for obtaining information on ADR. The manufacturer of the drug can also be a resource to consult.

13.0 WHEN TO REPORT ADVERSE DRUG REACTIONS

Report the event soon after it occurs. A recent event is easier to report and the report is more likely to be accurate.

If possible, take the decision to report while the patient is still with you, so that she/he can be readily probed about the event and all the details captured the reporting form immediately.

Send the report to the pharmacovigilance focal person within your facility, or if no such person exists, to the regional referral within your catchment or to an NDA office near you, or directly to the national Pharmacovigilance Centre at the NDA head office.:-

a) For reports on serious adverse events, within 24 to 48 hours of notification.

b) For non-serious adverse events report as soon as possible but in any case not later than 15 days

If you obtain any supplementary data for instance, if the same patient develops the reaction again, or if something happens which increases your suspicions or seems to exclude the reaction, send in this supplementary information immediately.

14.0 WHO SHOULD REPORT ADVERSE DRUG REACTIONS

All healthcare workers e.g. Doctors, Dentists, Pharmacists, Midwives, Nurses and Allied Health Professionals in Uganda should, as part of their professional responsibility report any suspected adverse drug reactions directly to the National Pharmacovigilance Centre offices or regional Pharmacovigilance Centres located in the regional referral hospitals as soon as possible within 15 calendar days after notification. Patients, caretakers, and the public should also report suspected adverse drug reactions.

15 HANDLING OF INFORMATION FROM YOUR REPORT

The information obtained from your reports helps to promote safe use of medicines on local, national and international levels. Your reported case will be entered into the National Adverse Drug Reaction database, and analysed by experts to determine possible casual relationships. Feedback will be given on the case as per procedures set by the NPC. A well completed adverse drug reaction reporting form submitted by you may result in one or more of the following:

a) Additional investigations into the medication in Uganda.

b) Educational initiatives to improve the safe use of medicines

c) Initiate a change in the schedule or manufacture of medicines to make them safer.

d) Regulatory and health promotion interventions as the situation may warrant including change in supply status or withdrawal.

Therefore, the purpose of ADR reporting is to reduce the risk associated with drug prescribing and administration and to ultimately improve patient care, safety and treatment outcome.

15.1 Benefits of Reporting

The health professional and patient stand to benefit as follows:

a) Improvement in the quality of care offered to patients.

b) Reduction of drug related problems leading to better treatment outcome.

c) Improve patient confidence in professional practice and consequently professional growth.

d) Improved knowledge.

e) Access to feedback information on drug related problems reported within the country and internationally.

f) Satisfaction for the fulfilment of a moral and professional obligation.

g) Improved Safety of Medicines in Uganda

15.2 Causality Classification

In order to assess the likelihood that the suspected adverse drug reaction is actually due to the drug, the WHO has provided a list of causality assessment criteria for deciding on the contribution of the drug towards the adverse event. The criteria is defined as follows:

15.1.1 Certain

a) Clinical event, lab test abnormality with plausible time relationship to drug intake.
b) Cannot be explained by concurrent disease or other drugs/ chemical.
c) Response to de-challenge- plausible
d) Event must be definitive pharmacological or immunologically.
e) Positive re-challenges (if performed)

15.1.2 Probable or Likely

a) Clinical event, lab test abnormality with reasonable time relationship to drug intake
b) Unlikely to be explained by concurrent disease, drugs/chemicals
c) Clinically reasonable response to withdrawal (de-challenge)
d) Re-challenge not required.

15.1.3 Possible

a) Clinical event, lab test abnormality with reasonable time relationship to drug intake
b) Could be explained by concurrent disease or other drugs or chemicals
c) Information on drug withdrawal may be lacking or unclear

15.1.4 Unlikely

a) Clinical event, lab test with improbable time relationship to drug intake
b) Other drugs, chemicals or underlying disease provide plausible explanations

15.1.5 **Inaccessible or unclassifiable:** Insufficient/contradictory evidence which cannot be supplemented or verified

15.1.6 **Conditional or unclassified**: More data is essential for proper assessment or additional data are under examination

In most cases, there is some level of uncertainty as to whether the drug is directly responsible for the reaction. Many of the questions may remain unanswered or may be contradictory; however, this should not stop you from reporting the reaction to the NPC.

16 MANAGEMENT SUPPORT TO PATIENT

The following are recommendations to consider while managing a patient with a suspected adverse drug reaction.

a) Assess the ADR and manage the patient accordingly
b) The suspected drug may be withdrawn
c) Medical treatment may be given
d) Patient may be referred to the next level of health care
e) Follow up the patient
f) Report the ADR.

In as much as possible, health facilities should have MTCs and or therapeutic review committees to review and inform the best course of management of ADRs.

17 HOW TO PREVENT ADVERSE DRUG REACTIONS

Most ADRs can be prevented by following the basic principles of rational use of medicines that are outlined below:

a) Use few drugs, whenever possible.
b) Use drugs that you know well.
c) Be aware of the interaction of drugs with certain foods, alcohol, traditional medicine and remedies and household chemicals.
d) Be particularly careful when prescribing to children and elderly, the pregnant and breastfeeding mothers, very ill patients with hepatic and renal diseases
e) Review all drugs used by your patient regularly, taking special notice with those bought without prescription.
f) If you suspect an ADR, consider stopping the drug or reducing the dosage as soon as possible

g) If the patient shows signs and symptoms not clearly explained by the course of the illness, think of an ADR

h) Do not change therapy from known to unfamiliar drugs without good reasons

18 HOW TO REPORT PRODUCT QUALITY PROBLEM

Notwithstanding adverse drug reactions, drugs on the market may present in a form that does not meet the specifications necessary for their intended purpose with regards to efficacy, copyright (counterfeit) and quality. Such Complaints on product quality and or efficacy can be reported manually by completing the market complaint form and submitting it to NDA. The forms can be accessed, filled and submitted online via the NDA website and at any of the NDA offices (regional and head office). Manual reports may also be scanned and sent to the corresponding addresses detailed out in this document

Note: Identities of the reporter and patient will remain strictly confidential.

19 SAFETYCOMMUNICATION

Risk communication refers to the exchange of real time information, advice and opinions between experts and people facing threats to their health, economic or social wellbeing. The fundamental goal of risk communication is to provide timely, meaningful, relevant and accurate information, in clear and understandable terms targeted to a specific audience for minimizing the risk burden.

Communicating safety information to patients and healthcare professionals is essential for achieving the objectives of pharmacovigilance. Promoting the rational, safe and effective use of medical products and minimizing risks contribute to the protection of patients and public health.

19.1 PRINCIPLES OF SAFETY COMMUNICATION

The following principles of safety communication shall be applied:

a) Safety communication shall deliver relevant, clear, accurate and consistent messages and reach the right audiences at the right time for them to take appropriate action.

b) Safety communication shall be tailored to the appropriate audiences (e.g. patients and healthcare professionals) by using appropriate language and taking account of the different levels of knowledge and information needs whilst maintaining the accuracy and consistency of the information conveyed.

c) The need for communicating safety information shall be considered throughout the pharmacovigilance and risk management process, and should be part of the risk assessment and risk minimization measures.

d) There should be adequate co-ordination and cooperation between the different parties involved in issuing safety communications (e.g. NMRAs, other public bodies and marketing authorization holders).

e) Information on risks shall be presented in the context of the benefits of the medicine and include available and relevant information on the seriousness, severity, frequency, risk factors, time to onset, reversibility of potential adverse reactions and expected time to recovery.

f) Safety communication shall address the uncertainties related to a safety concern. This is of particular relevance for new information which is often communicated while NMRAs are conducting their evaluations; the usefulness of communication at this stage needs to be balanced against the potential for confusion if uncertainties are not properly represented.

g) Information on competing risks such as the risk of non-treatment should be included where appropriate.

h) The most appropriate quantitative measures should be used when describing and comparing risks, e.g. the use of absolute risks and not just relative risks; when comparing risks, denominators should be the same in size. The use of other tools such as graphical presentation of the risk and/or the risk-benefit balance may also be considered.

i) Patients and healthcare professionals should, where possible, be consulted and messages pretested early in the preparation of safety communication, particularly on complex safety concerns.

j) Where relevant safety communication should be complemented at a later stage with follow-up communication e.g. on the resolution of a safety concern or updated recommendations.

k) The effectiveness of safety communication should be evaluated where appropriate and possible.

NB: SAFETY COMMUNICATIONS SHOULD COMPLY WITH RELEVANT REQUIREMENTS RELATING TO INDIVIDUAL DATA PROTECTION AND CONFIDENTIALITY.

19.0 REFERENCES

1. Uganda National Policy and Authority Act; Cap 206

2. Uganda National Policy and Authority (Pharmacovigilance) Regulations No. 37 of 2014.

3. Safety of Medicines, WHO/EDM/QSM/2002

4. Guideline for Adverse Drug Events Monitoring (Pharmacovigilance); Third Edition; Food, Medicine and Healthcare Administration and Control Authority of Ethiopia; Available on https://www.medbox.org/guideline-for-adverse-drug-events...ethiopia/download.pdf ; accessed on 19th/March/2018

5. Safety Monitoring of Medicines Products; Guidelines for setting up and running a Pharmacovigilance Centre; Uppsala Monitoring Centre- WHO Collaborating Centre for International Drug Monitoring

6. A practical handbook on pharmacovigilance of ant malarial medicines, WHO 2008

7. 9 October 2017 EMA/876333/2011 Rev 4* Guideline on good pharmacovigilance practices (GVP) Annex I - Definitions (Rev 4)

8. CIOMS Working Group VIII. Practical aspects of signal detection in pharmacovigilance. Council for International Organizations of Medical Sciences (CIOMS), Geneva, 2010

20.0 APPENDIX 1: NDA REGIONAL PHARMACOVIGILANCE CENTRES

Arua Regional Referral Hospital	The Director **Arua Regional Referral Hospital** P.O Box 03 Arua Uganda
Gulu Regional Referral Hospital	The Director **Gulu Regional Referral Hospital** P.O Box 160 Gulu Uganda Tel: 256(0)471432061, Fax 256(0)41250828 Email: gulurrhosp@gmail.com
Hoima Regional Referral Hospital	The Director Dr. Peter Mukobi **Hoima Regional Referral Hospital** P.O Box 05 Hoima Uganda Email: mukpet@gmail.com
Jinja Regional Referral Hospital	The Director Dr. Edward Nkurunziza **Jinja Regional Referral Hospital** P.O Box 43, Jinja Uganda Tel: 0772412498 Email: jinjahosp@utlonline.co.ug
Kabale Regional Referral Hospital	The Director Dr. Sophie Namasopo **Kabale Regional Referral Hospital** P.O BOX 07, Kabale Uganda Tel: 0772-470297 Email: snamasopo@gmail.com
Kabarole Regional Referral Hospital	Kyembamba Road Impala House 6th Floor, P.O.Box 47, Fort Portal, Uganda Tel:0483-422076
Lira Regional Referral Hospital	The Director **Lira Regional Referral Hospital** P.O Box 2,Lira Tel:+256 473 420 023/ +256 473 420 139
Masaka Regional Referral Hospital	The Director Dr. Nathan Onyachi **Masaka Regional Referral Hospital**

	P.O Box18 Alex Ssebowa Road, Masaka Tel: 0772433809 Email: onyachinathan@yahoo.com
Mbale Regional Referral Hospital	The Director, Dr. Emmanuel Tugaineyo **Mbale Regional Referral Hospital** P.O Box 921, Mbale, Uganda Tel: 0751519441/0773515601 Email: tituuza@gmail.com
Mbarara Regional Referral Hospital	The Director **Mbarara Regional Referral Hospital** P.O Box 40 Mbarara Uganda
Moroto Regional Referral Hospital	The Director Alfred Ogwang **Moroto Regional Referral Hospital** P.O Box 12 Moroto Uganda Tel: 0772454995 Email: ogwangaf@gmail.com
Mulago Regional Referral Hospital	The Director Dr. Birabwa-Male-Doreen **Mulago Regional Referral Hospital** Tel: 0772409944 Email: dbirabwamale@yahoo.com
Soroti Regional Referral Hospital	The Director **Soroti Regional Referral Hospital** P.O Box 289 Soroti, Uganda Tel: 0772435040/0774284949 Email: sorotihosp@yahoo.com

APPENDIX 2: ADDRESSES OF NDA REGIONAL OFFICES

a) **South-western Regional Office**

House No. 29, Mbaguta Estates, Kamukuzi; P.O. Box 1886; Tel. 0486-21088; MBARARA – UGANDA

b) **Western Regional Office**

Muganwa centre Plot 30, Old Toro Rd. P. O. Box 192; Tel/Fax 0465-440688; HOIMA – UGANDA

c) **Eastern Regional Office**

Busia/Malaba Entry Ports; P.O. Box 195; Mob. 0772-419136; TORORO – UGANDA, South Bukedi Cooperative Building; Plot No. 6 Busia Road; P.O. Box 453; Tel/Fax 045-45185; TORORO – UGANDA

d) **Northern Region Office Central Regional Office**:

Erute Road, P.O. Box 235; Tel. 0473-20652; LIRA – UGANDA

e) **Central Regional offices:**

Premier Complex Building; P.O. Box 23069; Tel. 0312-261548; NAKAWA – KAMPALA

f) **South Eastern Regional Office**:

Stanley Road; Jinja Municipality; P.O. Box 1710; Tel. 043-22176

g) West Nile Regional Office:

P. O. Box 1034; Plot No.1 mt. Wati road at Anyafio; Tel: 013 2266140, 031 2266141; ARUA

APPENDIX 3:

CONFIDENTIAL

Adverse event reporting ID Number:

REPORTING FORM FOR ALL SUSPECTED ADVERSE DRUG REACTIONS (ADR) AND ADVERSE EVENTS FOLLOWING IMMUNISATION (AEFI) – Use separate form for each event

Type of Report

Initial ☐ Follow up ☐ | Serious ☐ Not Serious ☐ | Drug ☐ Vaccine ☐ Herbal ☐ Others ☐

Patients Information

Patient ID/initials: _____ Gender: Male ☐ Female ☐ Weight (kg)_____ Pregnancy status Yes ☐ No ☐ N/A ☐

Full address_____ Telephone Number _____

*Date of birth :_ _/ _ _/ _ _ (dd/mm/yyyy) OR Age at onset:*_____ Medical History _____

Vaccine(s) Information

Vaccine						***Diluent (if applicable)***			
Name of vaccine	Date of vaccination	Time of vaccination	Dose (1st, 2nd, 3rd etc.)	Batch/Lot Number	Expiry date	Name of diluent	Batch/Lot Number	Expiry date	Date and time of reconstitution

Medical Product Details (List of all medicines used in the last 1 month (including herbals)**)**

Generic Name	**Brand name**	**Route**	**Dose and frequency**	**Date started**	**Date stopped**	**Indication**	**Tick suspected medicine**

Brief description of the ADR/AEFI and any treatment given	**Description of the AEFIs** *(for vaccines)* Severe local reaction > 3 days ☐ Encephalopathy ☐ Toxic shock syndrome ☐ Thrombocytopenia ☐ Anaphylaxis ☐ Generalized urticaria (hives) ☐ Injection site abscess ☐ High fever ≥38 °C ☐ Other (specify) _____

Date of ADR/AEFI onset: _ _ / _ _/_ _ _ _ Time of onset: _____ Date ADR/AEFI stopped: _ _ / _ _/_ _ _ _

Relevant laboratory test results

Reason for seriousness

Prolonged hospitalization ☐ Congenital anomaly ☐ Disability ☐ Death ☐ Life threatening ☐

Action taken

Drug withdrawn ☐ Dose increased ☐ Dose reduced ☐ Dose not changed ☐ Not applicable ☐ Unknown ☐

Outcome

Recovered ☐ Recovering ☐ Continuing ☐ Recovered with sequelae ☐ Not recovered ☐ Death ☐ Unknown ☐

Causality of the ADR/AEFI

Certain ☐ Probable/ Likely ☐ Possible ☐ Unlikely ☐ Unclassifiable ☐

Reporter details

Name of reporter:	E mail Address/Contact: Designation:	Date of reporting
Institution/Health facility:	Contact/Email:	District:

Administrative details

Report title:	Form ID number:	Date received:

APPENDIX 4: MEDICAL DEVICES ADVERSE EVENT/INCIDENT REPORTING FORM

Type of Report*
Initial ☐ Follow up ☐

Category of event*
Public health threat ☐ Death/Serious injury ☐ Other ☐

Date of Reporting: **Date of AE Onset:** **Date AE stopped:**

Patient information
Patient ID/initials: _____ Gender: Male ☐ Female ☐ Weight (kg)_____

Full address_____ Telephone Number _____

Date of birth :_ _/ _ _/ _ _ (dd/mm/yyyy) OR Age at event onset:_____

Patient history (co-morbidities and medication)_____ Pregnancy status Yes ☐ No ☐ N/A ☐

Device Information*

Brand name:		Serial/Lot No:
Common name: *(e.g. catheter, central venous, peripherally inserted)*	Model:	Catalogue:
Name of manufacturer:	Address:	

Operator of device at time of onset
Healthcare Professional ☐ Patient ☐ Caregiver ☐ N/A ☐

Usage of device *(choose whichever applies)*
Single use ☐ Reuse of Reusable ☐ Reuse of single use ☐ Reserviced/Refurbished ☐

Problem noted prior to use ☐ other (specify) ☐ _____

Date of Implant: Date of Explant:

Device Disposition/Current location:	Expiry date *(if applicable)*:

Diagnostics section *(for diagnostics only)*

Type of specimen used (e.g. blood, saliva, etc):		
No. of patients involved:	No. of tests done:	No. of false positives:
No. of false negatives:	No. of true positives:	No. of true negatives

List of other devices involved in the event*

Description of Event

Remedial Action/Corrective Action/Preventive Action

Patient Outcome*

Continued ☐ Recovered ☐ Recovering ☐ Disability ☐ Death ☐

Details of reporter*

Name of reporter: **Email/contact:** **Designation / Occupation:**

Name of institution: Location address:

22. DOCUMENT REVISION HISTORY

Date of revision	Revision number	Document Number	Author(s)	Changes made and/or reasons for revision
24 October 2019	01	Doc. No. DPS/GDL/013	Julius Mayengo	This is the first scheduled review

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