MEDICINES CONTROL AGENCY

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GUIDELINE FOR SAFETY MONITORING OF MEDICINES(PHARMACOVIGILANCE) INCLUDING VACCINES

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1 INTRODUCTION

1.1 LEGAL BASIS

1.1.1. The regulation of medicines in The Gambia is governed by the provisions and requirements of the Medicines and Related Products Act, 2014 ("Act"), by which the Medicines Control Agency (MCA) was established as the regulatory body for medicines and related products.

1.1.2. Part II Sections 4 (c) requires the Agency to ensure that evidence of existing and new adverse events, interactions and information about pharmacovigilance of medicines being monitored globally, are analysed and acted upon.

1.1.3. The Medicines and Related Products Regulations, 2020 ("Regulations") details the legal requirements.

1.1.4. MCA functions as the National Pharmacovigilance Centre. Safety monitoring of medicines by the Agency ensures that they continue to be safe for patients and the general public. Healthcare professionals, marketing authorisation holders (MAHs) or their national representatives and manufacturers are key stakeholders in the continuous safety monitoring of medicines marketed in The Gambia.

1.2 INTERPRETATION AND ABBREVIATIONS

Interpretations and abbreviations contained in the MCA Glossary can be found on the MCA Website: **www.mca.gm.**

The interpretation of terms provided in the Act and Regulations apply, unless further defined in this guideline.

Abuse
The persistent or sporadic, intentional excessive use of a medicine, which is accompanied by harmful physical or psychological effects

Adverse Drug Reaction (ADR) Case Report
A case report in pharmacovigilance is a notification related to a patient who has experienced an adverse medical event or laboratory test abnormality suspected to be induced by a medicine. It is important to stress that healthcare professionals should send reports of ADRs even if they do not have all the information required.

Adverse Event/Experience
Any unwanted medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment. The basic point here is that an unwanted event occurs during or after the use of a medicine; the time of occurrence may be related to the use of the medicine but the event is not necessarily caused by it.

Adverse Event Following Immunisation (AEFI)
Any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.

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

Consumer
A person who is not a healthcare professional such as a patient, friend or relative of the patient or any member of the public.

Expedited Reporting
Is the immediate reporting of a serious adverse reaction to the Agency in not more than the certain required time period.

Healthcare professional (Health professional, Health practitioner)
A person who is a medically qualified person such as a physician, dentist, pharmacist, or nurse.

Marketing Authorisation Holder
An organisation that has been issued a licence by the competent authority to market a medicine, medical equipment, or cosmetics within The Gambia or any other country and may or may not be the manufacturer of the particular product.

Individual Case Safety Report (ICSR); synonym: Adverse (Drug) Reaction Report
Format and content for the reporting of one or several suspected adverse reactions to a medicine that occur in a single patient at a specific point of time.

ICSRs shall be used for collection, processing, quality control, coding, classification, medical review and reporting suspected adverse reactions to a medicine that occur in a single patient at a specific point in time. The source for an ICSR could also be the literature, clinical study or post-authorization safety study.

Medication Error
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.

Misuse
Situations where the medicine is intentionally and inappropriately used not in accordance with the terms of the marketing authorisation.

New Drug / Medicine
A chemical or biologically active pharmaceutical ingredient that has not previously been issued with a marketing authorisation as an ingredient in any pharmaceutical product in The Gambia.

Off-label use
Situations where the medicine is intentionally used for a medical purpose not in accordance with the authorised product information.

Overdose
The administration of a quantity of a medicine given per administration or cumulatively, which is above the maximum recommended dose according to the authorised product information.

Periodic Benefit Risk Evaluation Report (PBRER)
An update of the world-wide marketing experience of a product at defined times with focus on formal evaluation of benefit in special population at defined times during post-registration period.

Periodic Safety Update Report (PSUR)
A regular update of the world-wide safety experience of a product at defined times during post registration period.

Post Authorisation Safety Study (PASS)
Any study relating to an authorised product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the product, or of measuring the effectiveness of risk management measures.

Qualified Person for Pharmacovigilance (QPPV)
An individual named by a Marketing Authorisation Holder (MAH) and approved by the Agency as the person responsible for ensuring that the company (the MAH) meets its legal obligations for monitoring of the safety of the product marketed in The Gambia.

Risk Benefit Balance
An evaluation of the positive therapeutic effects of the medicine in relation to the risks (any risk relating to the quality, safety or efficacy of the medicine as regards patients' health or public health).

Risk Management Plan
A systematic approach and set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicines, and the assessment of effectiveness of those interventions and how these risks will be communicated to the Agency and the general population.

Serious Adverse Event or Reaction (SAE/SAR)
Any untoward medical occurrence that at any dose:

- results in death, or
- is life-threatening, or
- requires inpatient hospitalisation or prolongation of existing hospitalisation, or
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly (birth defect), or
- is otherwise medically important event or reaction (e.g. that it does not meet preceding criteria, but is considered serious because treatment/intervention would be required to prevent one of the preceding criteria).

Note: The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/reaction which hypothetically might have caused death if it were more severe.

Side Effect
Any unintended effect of a pharmaceutical product occurring at doses normally used in human, which is related to the pharmaceutical properties of the medicine. Such effects may or may not be beneficial. Side effects are

related to the known properties of the medicine and can often be predicted. It must be stressed that in pharmacovigilance, interest lies in all medicine related reactions, this includes side effects and suspected adverse drug reactions. Healthcare professionals must therefore report all medicine related problems to the National Pharmacovigilance Centre (NPC) at the Agency.

Signal
Refers to "Reported information on a possible causal relationship between an adverse event and a medicine; the relationship being known 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.

Spontaneous Report or Spontaneous Notification
Unsolicited voluntary communication by a patient, consumer, healthcare professional, marketing authorisation holder or national representative or an organisation to the Agency that describes a suspected adverse reaction in a patient or consumer who is given one or more medicines and which is not derived from a study or any organised data collection systems where adverse event reporting is actively sought.

Unexpected adverse reaction
An adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorisation, or expected from the characteristic of the medicine.

Pharmacovigilance
The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problem.

1.3 PURPOSE AND SCOPE

1.3.1. The objective of safety monitoring is to assess and monitor risks related to the utilisation of medicines including vaccines in humans, to implement measures to reduce such risks and to promote the proper and safe use of these medicines.

1.3.2. In pursuance of the law this document provides guidance on the continuous safety monitoring of medicines marketed in The Gambia to ensure they continue to be safe for patients and the general public, and on communication of safety information on medicines.

1.3.3. This guideline applies to medicines as defined in the Act and the Regulations including biologicals (e.g. vaccines, blood and blood components), herbal medicines, radiopharmaceutical products and nutritional supplements.

1.3.4. It applies to marketing authorisation holders (MAHs) or their national representatives (local or regional agent), manufacturers and other pharmacovigilance stakeholders.

1.3.5. For expedited reporting of adverse reactions to medicines or other safety issues including product quality defects refer to MCA *Guideline for Reporting of Adverse Reactions to Medicines including Vaccines* (MCA-GL-305).

2 ROLES AND RESPONSIBILITIES

2.1 MARKETING AUTHORISATION HOLDER (MAH)

2.1.1 Qualified Person for Pharmacovigilance (QPPV)

2.1.1.1. MAHs of medicines marketed in The Gambia shall permanently and continuously have at their disposal a person who is responsible for Pharmacovigilance, referred to as Qualified Person for Pharmacovigilance (QPPV).

Qualifications of QPPV

2.1.1.2. The QPPV shall be an employee of the MAH. Where it is not possible for the MAH to be the employer of the QPPV, the national representative or local importer shall serve as the employer of the QPPV. Each national representative or local importer may appoint one QPPV to cover all the relevant products for his business.

2.1.1.3. This person shall be a healthcare professional registered with the relevant statutory health council in The Gambia and being formally trained in pharmacovigilance by MCA or an institution recognised by the Agency.

2.1.1.4. The person designated as QPPV shall be a healthcare professional with BSc Medicine, B. Pharmacy, BSc. Nursing, or any other healthcare professional degree recognised by the Agency.

2.1.1.5. The Agency may also accept a person with a university degree in a relevant scientific discipline with at least two years minimum experience with specific job function in the area of pharmacovigilance for designation as the QPPV.

Responsibilities of QPPV

2.1.1.6. The responsibilities of the QPPV shall include but not limited to the following:

- Act as a point of contact for the Agency on all matters relating to pharmacovigilance and safety of marketed products including inspections.
- Establish and maintain a system which ensures that information about all suspected adverse reactions/events are collected, collated, processed and forwarded to the Agency and where applicable to the MAH.
- Prepare and submit to the Agency:
    - Adverse Reaction reports as Individual Case Safety Reports (ICSRs);
    - Periodic Safety Update Reports (PSURs) or Periodic Benefit-Risk Evaluation Reports (PBRER), as applicable.
    - Risk Management Plans, where applicable. All RMPs submitted shall be signed by the QPPV. The signature shall mean that the QPPV has read the RMP and will ensure implementation of all activities outlined in the RMP.

- Ensure that any request from the Agency for additional information deemed necessary for the evaluation of the risk-benefit ratio of a marketed product is provided to the Agency promptly and fully.
- Oversee the safety profiles of the company's marketed products and any emerging concerns.

2.1.2 Safety Monitoring and Reporting

2.1.2.1. MAH of medicines marketed in The Gambia or their national representative or local importer shall have in place an appropriate system of safety monitoring to ensure that appropriate action can be taken when necessary.

2.1.2.2. MAH of medicines marketed in The Gambia or their national representative or local importer should ensure to monitor constantly the risks of its medicine and to report the results of this monitoring to the Agency.

2.1.2.3. MAH of medicines marketed in The Gambia or their national representative or local importer should take all appropriate actions to minimise the risks of the medicines and maximise the benefits including ensuring the accuracy of all information produced in relation to their medicines, and actively updating and promptly communicating it when new information becomes available.

2.1.2.4. MAH of medicines marketed in The Gambia or their national representatives shall:

- inform the Agency of any new or existing quality, safety or effectiveness concerns related to any medicine, including but not limited to adverse reactions;
- inform the Agency of any risk management activities;
- maintain a pharmacovigilance master file and make it available on request;
- evaluate all of the information, examine risk minimisation and prevention measures and, where necessary, take risk minimisation and prevention measures immediately based on its pharmacovigilance system;
- audit its pharmacovigilance system regularly at appropriate intervals; and make a note of the important findings in its pharmacovigilance master file and ensure that corrective measures are taken to remedy deficiencies before the note is deleted from the pharmacovigilance master file;
- operate a risk management system for every medicine authorised and monitor the outcome of risk minimisation measures that are part of the risk management plan or as requested by the Agency; and
- update the risk management system and monitor pharmacovigilance data to determine whether there are any new risks, whether the risks have changed or whether there are any changes to the risk-benefit balance of medicines.

2.1.2.5. MAH of medicines marketed in The Gambia or their national

representative or local importer shall keep a record of all suspected adverse reactions and the quantities supplied.

2.1.2.6. MAH of medicines marketed in The Gambia or their national representative or local importer shall submit Individual Case safety Reports (ICSRs) on suspected serious adverse reactions to a medicine that occurred in The Gambia in accordance with the requirements as stipulated in the MCA *Guideline for Reporting of Adverse Reactions to Medicines including Vaccines* (MCA-GL-305).

2.1.2.7. MAH of registered medicines in The Gambia or their national representative or local importers shall communicate any of the following information immediately but not later than within 15 calendar days to the Agency:

- Information that contradicts information already furnished to the Agency;
- Information that indicates that the use of the registered medicine in accordance with the recommendations for its use may have an unintended harmful effect; and
- Information that the registered medicine, when used in accordance with the recommendations for its use, may not be effective in relation to information submitted previously.

2.1.2.8. A report of lack of therapeutic efficacy for a life-threatening infection, which appears to be due to the development of a newly resistant strain of an infective agent previously regarded as susceptible, should be submitted as ICSR.

2.1.2.9. Lack of prophylactic efficacy of vaccines may highlight potential signals of reduced immunogenicity in a sub-group of vaccines, waning immunity, or strain replacement. Such a signal may need prompt action and further investigation through post-authorisation efficacy studies as appropriate.

2.1.2.10. Any matter relating to the safety of the medicine, withdrawal or suspension of availability of the medicine, the addition of a contraindication or the modification for safety reasons of an existing contraindication, warning or precaution statement in the approved product information must be communicated to the Agency.

2.1.2.11. MAH of registered medicines in The Gambia or their national representative or local importer shall not make any pharmacovigilance information public without notifying the Agency and shall ensure that such information presented is not false or misleading.

2.1.2.12. Non-adherence to the requirements of this guideline by the marketing authorisation holders or national representatives or local importers may result in sanctions imposed by the Agency.

2.1.3 Requirements regarding the Pharmacovigilance System

2.1.3.1. Applicants for marketing authorisation are required to provide a summary of their pharmacovigilance system, in accordance with the Regulations, which they will introduce once the authorisation is granted.

2.1.3.2. The summary of the pharmacovigilance system should be provided in the application dossier for marketing authorisation (see Module 1.8.1 of the

EU Notice to Applicants, Pharmacovigilance System) and include the following elements:

- proof that the applicant has at his disposal a qualified person responsible for pharmacovigilance (QPPV);
- the location in which the QPPV resides and carries out his/her tasks;
- the contact details of the QPPV;
- a statement signed by the applicant to the effect that the applicant has the necessary means to fulfil the tasks; and
- a reference to the location where the pharmacovigilance system master file (PSMF) for the medicines is kept.

2.1.3.3. The MAH may combine this information in one single statement to confirm the obligation to have the necessary means to fulfil the tasks and responsibilities listed in this document.

2.1.3.4. Such statement should be signed by an individual who can act on behalf of the legal entity of the applicant/MAH and by QPPV. The title, role and responsibility of each individual signing the statement should be clearly specified in the document.

2.1.3.5. The requirement for the summary of the pharmacovigilance system is the same for any marketing authorisation application, independent of the legal basis for the application.

2.1.4 Requirements regarding Pharmacovigilance System Master File (PSMF)

2.1.4.1. The MAH has to operate a pharmacovigilance system for the fulfilment of his pharmacovigilance tasks. The pharmacovigilance system master file (PSMF) is a detailed description of the pharmacovigilance system used by the MAH with respect to one or more authorised medicines.

2.1.4.2. The PSMF is not part of the registration/marketing authorisation (MA) dossier and is maintained independently from the MA.

2.1.4.3. It should be permanently available for inspection and should be provided within 15 days to the Agency, if requested.

2.1.4.4. The PSMF must be located either at the site where the main pharmacovigilance activities of the MAH are performed or at the site where the QPPV operates. The QPPV should reside in The Gambia and could operate nationally or internationally.

2.1.4.5. Applicants are required, at the time of initial MA application (MAA), to have in place a description of the pharmacovigilance system that records the system that will be in place and functioning at the time of granting of the MA and placing of the product on the market.

2.1.4.6. During the evaluation of a MAA the applicant may be requested to provide a copy of the PSMF for review. The PSMF has to describe the pharmacovigilance system in place at the current time.

2.1.4.7. Information about elements of the system to be implemented in future may be included, but these should be clearly described as planned rather than established or current.

2.1.4.8. The pharmacovigilance system will have to be in place and functioning at the time of granting of the MA and placing of the product on the market.

2.2 MEDICINES CONTROL AGENCY (MCA)

2.2.1. With the aim to fully assess the benefit/risk profile the Agency may ask the MAH to provide additional data on safety, efficacy or quality of authorised medicines, if it is necessary from a public health perspective.

2.2.2. The following measures may be aimed at collecting or providing data to enable the assessment of the safety or efficacy of medicines in the post-approval setting:

- PV system plan including PSUR/PBRER, and
- RMP to be presented at the time of MA application as a part of the registration application dossier.

2.2.3. Additionally, the Agency may request or impose the MAH/sponsor:

- pharmacovigilance activity in the RMP (non-clinical studies, CTs or non-interventional PASS/PAES which are required to investigate a safety concern of a medicines to be listed in the pharmacovigilance plan of the RMP and are either aimed at identifying and characterising risks, or at assessing the effectiveness of risk-minimisation activities. The MAH has the obligation to provide the requested data within the stated timeframes. Once additional pharmacovigilance activities have been agreed within the RMP, changes to these measures (e.g. proposals for adjusting due dates of agreed milestones, proposals to change the scope of agreed study or its duration, etc.) should be submitted via the appropriate variation procedure to amend the RMP.)
- specific obligation - imposed on MAs granted under exceptional circumstances or for medicines with conditional MA (e.g. providing interim results of the additional interventional/non-interventional studies, data on special populations).
- legally binding measures (e.g. cumulative review following a request originating from a PSUR or a signal evaluation, Corrective Action/Preventive Action (CAPA).

2.2.4. The Agency may issue recommendations for further development of the medicine, e.g. quality improvement, update patient information leaflets or SmPC. This information might be submitted as a variation application as appropriate, if it impacts the authorised medicine and its product information.

2.2.5. MCA shall receive all reports on safety issues of medicines and be responsible for the review, categorisation and follow-up of reports and any other safety information.

2.2.6. To prevent direct or indirect hazards to human health, the Agency shall:

- record and evaluate risks associated with the administration of medicines;
- record suspected cases of adverse reactions to medicines, interactions with other products, and adulterations and-

- monitor the outcome of the risk minimisation measures contained in the risk management plans, and
- assess updates to the risk management system; and

- co-ordinate the measures to be adopted to address any risks in accordance with the legal requirements.

2.2.7. The Agency shall acknowledge the receipt of PSURs or PBRERs and communicate preliminary evaluation comments to the MAH or the national representative within 28 calendar days of receipt of the report.

2.2.8. The Agency shall evaluate and transmit the evaluation reports of PSURs or PBRERs to the Medicines Safety Experts Committee (MSEC) for review and recommendations.

2.2.9. Based on the recommendations of the MSEC, the Agency shall determine whether there are new risks, whether the risks have changed and whether there are changes to the risk-benefit balance of medicines and shall take the necessary measures.

2.2.10. The Agency may instruct the initiation of studies or research to investigate safety concerns, and shall authorise and review such studies as detailed in the MCA *Guideline for Clinical trials in Humans*.

2.2.11. The Agency shall inform the public about medicines that pose health risks and measures that have been developed to mitigate the risks.

2.2.12. The Agency shall cooperate with the World Health Organization and other regional and international medicines regulatory authorities that keep records on medicines risks and communicates ICSR reports to the Uppsala Monitoring and Collaborating Centre, a WHO Programme for International Drug Monitoring

3 PERIODIC SAFETY UPDATE REPORT (PSUR) / PERIODIC BENEFIT-RISK EVALUATION REPORT (PBRER)

3.1. A Periodic Safety Update Report (PSUR) or Periodic Benefit-Risk Evaluation Report (PBRER) is to present a comprehensive, concise, and critical analysis of new or emerging information on the risks of the medicine and on its benefits in approved indications to enable a product's overall benefit-risk profile.

3.2. MAHs of both innovator and generic medicines or their national representatives are required to submit PSUR or PBRERs to the Agency.

3.3. A PSUR is intended to provide an update of the worldwide safety experience of a medicine.

3.4. The PBRER shall include:

- a summary of the data that is of interest to assess the benefits and risks of a medicine, including the results of all studies that can have an effect on the marketing authorisation;
- a scientific evaluation of the medicine's risk-benefit balance based on all of the available data, including data from clinical trials for therapeutic

indications and population groups that are not covered by the marketing authorisation; and

- data related to the medicine's volume of sales and any other relevant to the volume of prescriptions, including an estimate of the number of persons using the medicines.

3.5. The Agency accepts PSUR or PBRER in the format recommended by ICH E2C Guidelines and E2C (R2), respectively.

3.6. The frequency for the submission of PSUR or PBRERs shall be as follows, if not stated otherwise in the marketing authorisation:

- where a medicine has not yet been placed on the Gambian market, at least every six months after the marketing authorisation has been granted and until it is placed on the market;
- where a medicine has been placed on the Gambian market, at least every six months during the first two years after it is first placed on the Gambian market and once a year after two years and three-yearly intervals thereafter.

3.7. The Agency may also request for an ad hoc PSUR or PBRER outside the specified reporting requirements when there are new risks, when risks have changed, when efficacy/effectiveness has changed or when there are changes to the benefit-risk profile of a medicine.

3.8. Each PSUR or PBRER should cover the period of time since the last PSUR or PBRER and should be submitted within 60 days after the Data Lock Point (DLP).

3.9. For medicines with marketing authorisation in different countries, the MAH may synchronise the Local Birth Date (LBD) with the International Birth Date (IBD). The Agency will accept a single harmonised IBD and DLP for each medicine in order to reduce the burden of work in preparing PSURs or PBRERs for different regulatory authorities.

4 RISK MANAGEMENT PLAN

4.1. The Risk Management Plan (RMP) details the known safety concerns with the medicine and how they can be managed. It also includes details of any additional studies that have been recommended at the time of licensing to provide more information on the medicine's safety profile.

4.2. The overall aim of risk management is to ensure that the benefits of a particular medicine exceed the risks by the greatest achievable margin for the individual patient and for the target population as a whole.

4.3. The RMP should contain the following elements which:

- identify or characterise the safety profile of the medicine(s) concerned;
- indicate how to characterise further the safety profile of the medicine(s) concerned;
- document measures to prevent or minimise the risks associated with the medicine(s) including an assessment of the effectiveness of those interventions;

- document post-authorisation obligations that have been imposed as a condition of the marketing authorisation;
- describe what is known and not known about the safety profile of the concerned medicine(s);
- indicate the level of certainty that efficacy shown in clinical trial populations will be seen when the medicine is used in the wider target populations seen in everyday medical practice and document the need for studies on efficacy in the post-authorisation phase (also known as effectiveness studies); and
- include a description of how the effectiveness of risk minimisation measures will be assessed.

4.4. The structure of the RMP should follow the European Good pharmacovigilance Practices (GVP) Module V – Risk management systems and contain a safety specification in accordance with ICH Guideline for Pharmacovigilance Planning (E2E).

Structure of the RMP

4.5. The RMP consists of seven parts as listed below; certain parts specifically the Safety specification are subdivided into modules so the content can be tailored to the specifics of the medicine and modules added/ removed or re-used in other documents (e.g. PSURs). RMP part II modules generally follow the section titles in the Safety Specification of ICH-E2E, whilst RMP part III follows the Pharmacovigilance Plan.

Part I: Product(s) overview

Part II: Safety specification

Module SI: Epidemiology of the indication(s) and target population(s)

Module SII: Non-clinical part of the safety specification

Module SIII: Clinical trial exposure

Module SIV: Populations not studied in clinical trials

Module SV: Post-authorisation experience

Module SVI: Additional requirements for safety specification not discussed in ICH-E2E (e.g. off-label use, misuse and abuse, transmission of infectious disease, medication error)

Module SVII: Identified and potential risks

Module SVIII: Summary of the safety concerns

Part III: Pharmacovigilance plan

Part IV: Plans for post-authorisation efficacy studies

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation measures)

Part VI: Summary of the risk management plan

Part VII: Annexes

4.6. For detailed description of each part of the RMP and the format acceptable to the Agency, MAHs or their national representative are directed to read GVP Module V – Risk management systems by EMA.

4.7. If the RMP is submitted as part of the registration/marketing authorisation application, cross references to other parts of the dossier should be avoided since it is intended that the RMP should be a largely stand-alone document.

4.8. An update, as applicable, may need to be submitted at any time during a medicine's lifecycle when requested by the Agency or when the MAH identifies a safety concern with a medicine at any stage of its life cycle.

4.9. The submission of a RMP may not be required for the marketing authorisation of a generic medicine where no safety concern requiring additional risk minimisation activities has been identified with the reference medicine.

5 POST-AUTHORISATION SAFETY AND EFFICACY STUDIES

5.1. Post-authorisation safety studies (PASS) and post-authorisation efficacy studies (PAES) may be conducted voluntarily by the MAHs of medicines marketed in The Gambia or their national representative or requested by the Agency to be conducted by the MAH or national representative. A PASS or PAES may be interventional or non-interventional.

5.2. The recommendations as laid down in the European guidelines for PASS and PAES should be taken into consideration.

5.3. A **PASS** may be initiated under the following conditions:

- As a condition to the granting of the marketing authorisation, or after the granting of a marketing authorisation if there are concerns about the risks of the authorised medicine;
- As part of a marketing authorisation granted under exceptional circumstances; or
- Required in the risk management plan to investigate a safety concern or evaluate the effectiveness of risk minimisation activities

5.4. A **PAES** may be initiated under the following conditions:

- An initial efficacy assessment based on surrogate endpoints requires verification;
- In the case of medicines used in combination with other medicines, there may be a need for further efficacy data to clarify uncertainties;
- Uncertainties with respect to the efficacy of a medicine in certain subpopulations that could not be resolved prior to marketing authorisation;
- A change in the understanding of the standard of care for a disease or the pharmacology of a medicine;
- The potential lack of efficacy in the long term that raises concerns with respect to the maintenance of a positive benefit-risk balance of the medicine; or

- New concrete and objective scientific factors that may constitute a basis for finding that previous efficacy evaluations may need to be significantly revised.

5.5. A **PASS** should be conducted with the following objectives:

- Quantify potential or identified risks, e.g. to characterise the incidence rate, estimate the rate ratio or rate difference in comparison to a non-exposed population or a population exposed to another medicine or class of medicines, and investigate risk factors and effect modifiers;
- Evaluate risks of a medicine used in patient populations for which safety information is limited or missing (e.g. special populations - pregnant women, specific age groups, patients with renal or hepatic impairment);
- Assess patterns of medicine utilisation that add knowledge on the safety of the medicine (e.g. indication, dosage, co-medication, medication errors);
- Measure the effectiveness of a risk minimisation activity;
- Evaluate the risks of a medicine after long-term use; or
- Provide evidence about the absence of risks.

5.6. MAHs or their national representatives shall report to the Agency any PASS or PAES that will be conducted in The Gambia voluntarily.

5.7. The MAHs or their national representatives are responsible for the financing and conduct of PASS or PAES in The Gambia.

5.8. The requirements for clinical trials or non-interventional/observational clinical studies, where applicable, as stipuletaed in the MCA *Guideline for Clinical Trials in Humans* (MCA-GL-501) apply.

5.9. The Agency may require the submission of progress reports during the conduct of the PASS or PAES.

5.10. The MCA *Guideline for Reporting of Adverse Reactions to Medicines* (MCA-GL-305) applies, unless the Agency specifies different requirements for the PASS.

5.11. The Agency shall transmit the draft of the observation plan (protocol) to the MSEC for evaluation and recommendations and authorise the conduct of PASS or PAES based on the recommendations of the Committee.

5.12. MAHs or their national representatives or local importer shall not conduct a PASS or PAES if:

- the medicine under observation is not marketed in The Gambia;
- the study promotes the use of the medicine;
- payments for the participation of the healthcare professionals involved is not restricted to compensation for time and expenses incurred; and
- an incentive is created for the preferential prescription or recommendation of specific medicines.

6 SAFETY COMMUNICATION

6.1. Throughout the life cycle of the medicine including vaccine information relating to the benefit-risk profile of the product may need to be communicated to stakeholders including, regulatory authorities and marketing authorisation holders, patients and healthcare professionals who use (e.g. prescribe, handle, dispense, administer or take) medicines.

6.2. Safety communication aims at:

- providing timely evidence-based information on the safe and effective use of medicines;
- facilitating changes to healthcare practices (including self-medication practices) where necessary;
- improving attitudes, decisions and behaviour in relation to the use of medicines;
- supporting risk minimisation behaviour;
- facilitating informed decisions on the rational use of medicines.
- support public confidence in the regulatory system.

6.3. The message must be transmitted, received and understood by the target audience to be effective in the way it was intended, and appropriate action is taken by the target audience.

6.4. All Safety Communication issued by the MAHs or their national representatives or manufacturers or local importers shall receive prior approval from the Agency. Application for approval shall include a copy of the proposed communication, the medium of distribution and the targeted audience(s).

6.5. Types of Safety Communication can be as follows:

- Direct healthcare professional communication;
- Documents in lay language for patients;
- Press communication or press releases;
- Websites;
- Bulletins and newsletters; or
- Responding to enquiries from the public.

6.6. Safety communication should contain:

- important emerging information on any medicine which has an impact on the medicine’s benefit-risk balance under any conditions of use;
- the reason for initiating safety communication clearly explained to the target audience;
- any recommendations to healthcare professionals and patients on how to deal with a safety concern;
- when applicable, a statement on the agreement between the marketing authorisation holder or national representative and the Agency on the safety information provided;

- information on any proposed change to the product information (e.g. the summary of product characteristics (SmPC) or package information leaflet (PIL);
- a list of literature references, when relevant or a reference to where more detailed information can be found; and
- where relevant, a reminder of the need to report suspected adverse reactions in accordance with MCA *Guideline for Reporting of Adverse Reactions to Medicine*.

7 SAFETY MONITORING DURING PUBLIC HEALTH EMERGENCY

7.1. It is highly important to provide access to safe and efficacious medicines during public health emergency, including pandemics (e.g. COVID-19), any significant outbreaks of infectious disease or bioterrorist attacks. The preventive measures and managing procedures that will be implemented by the Agency in response to such public health threats are described further.

7.2. Safety monitoring plan with a focus on active pharmacovigilance will be implemented. This will ensure reporting of ARs associated with medicines authorised for Emergency Use to facilitate early detection of safety signals and to promote patient safety.

7.3. Emergency Use Authorisation (EUA) procedure will be realised in accordance with the national requirements. A risk-benefit approach will be used for assessing and listing unlicensed medicines for use primarily during public health emergencies of international concern (PHEIC) or any other/national public health emergencies. The European Medicines Agency (EMA) and the WHO recommendations and the WHO Essential Medicines List will be used as a guiding reference.

7.4. The approval of any medicine(s) or diagnostics for EUA is not intended to interfere with ongoing clinical trials. This means that the clinical development should proceed as planned after the initial submission and subsequent updates.

7.5. All adverse drug reactions (ADRs) including therapeutic failures for medicines being used for treatment of diseases defined as public health emergency should be reported within 24 hours of detection. In addition, information on lack of efficacy, medication errors, use out of specification, use in pregnant/breastfeeding women, newborns and children should be reported in priority. Additional attention should be paid to the Events of Special Interest. Pregnancy outcome to be followed up accordingly.

7.6. The initial report on the suspected adverse reaction must contain:

- suspected medicines;
- the age and gender of the patient;
- description of the adverse reaction (including indication of seriousness);
- patient's medical history (including any previously diagnosed/recently diagnosed conditions);
- any concomitant medications, whether supportive or already prescribed;

- outcome of the reaction (resolved, revolving, death);
- statement whether medicine was discontinued as a result of the adverse reaction.

7.7. AR and AEFI reports should be submitted to the Agency using the respective reporting form available from the MCA website: www.mca.gm and be sent to MCA by email: info@mca.gm.

7.8. Adverse reaction reporting forms will be distributed to all relevant health facilities recognised by the Ministry of Health.

7.9. The MCA will follow up on the Heads of the institutions or health facilities to report weekly. These reports should be accompanied by completed AR or AEFI reporting forms, where applicable.

7.10. All the reported ARs and AEFIs are to receive immediate attention of the PV Focal Person at the Agency.

7.11. AR and AEFI reports will be submitted for a review by the MSEC. The assessment of these ADR and AEFI reports will be prioritised by the MSEC to ensure that any new safety concerns are managed appropriately, with information communicated as quickly as possible for continued safe and effective use of these products.

8 ADDITIONAL MEASURES

8.1. Emerging Safety Issues (ESIs) - are safety issues considered by a MAH to require urgent attention by the Agency because of the potential major impact on the risk-benefit balance of the medicines and/or on patients' or public health and is to be closely monitored.

8.2. Training for healthcare professionals on the use of the recommended medicines, medicines safety aspects and reporting of ADRs will be provided by MCA. Refer to the MCA *Guideline for the National Pharmacovigilance System* (MCA-GL-308).

8.3. The officers in-charge in the health facilities are responsible for submitting AR and AEFI reports to the Regional Focal Person for Pharmacovigilance for onward transmission to MCA, if not submitted directly by the reporter to the Agency.

8.4. Interaction with institutions and stakeholders involved in the research and development of medicines and public health authorities within the country is established. The rapid exchange of information on pharmacovigilance issues between the Agency and stakeholders will take place through established communication channels such as website. Refer to the MCA *Guideline for the National Pharmacovigilance System* (MCA-GL-308).

8.5. Interactions with international partners, regulatory agencies and public health authorities (WHO, PEI, BfArM, FDA Ghana, MCAZ, WAHO, etc) are ongoing. Discussion on specific scientific and regulatory topics take place as necessary in accordance with the framework described above and in compliance with the recognition & reliance measures and confidentiality agreements.

9 FINAL PROVISIONS

8.1. This guideline is the first version published by the MCA and will become effective on 10 December 2021.

8.2. This guideline will be reviewed within 5 years of becoming effective.

10 DOCUMENTS NEEDED FOR THIS GUIDELINE

None

11 REFERENCES

- Medicines and Related Products Act, 2014
- Medicines and Related Products Regulations, 2020
- EMA. Guideline on good pharmacovigilance practices (GVP) Module VII – Periodic safety update report (EMA/816292/2011 Rev 1), 9 December 2013
- ICH Harmonised Tripartite Guideline, Periodic Benefit-Risk Evaluation Report (PBRER) E2C(R2), 17 December 2012
- EMA. Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (EMA/838713/2011 Rev 2), 28 March 2017
- ICH Harmonised Tripartite Guideline, Pharmacovigilance Planning (E2E). 18 November 2004
- EMA. Guideline on good pharmacovigilance practices (GVP) Module VIII – Post-authorisation safety studies (EMA/813938/2011 Rev 3), 9 October 2017
- EMA. Scientific guidance on post-authorisation efficacy studies (EMA/PDCO/CAT/CMDH/PRAC/CHMP/261500/20150), 12 October 2016
- EMA. Guideline on good pharmacovigilance practices (GVP) 3 Module XV – Safety communication (EMA/118465/2012), 26 July 2012
- European Commission, Volume 2B Notice to Applicants, Medicinal products for human use, Presentation and format of the dossier, Common Technical Document (CTD), Module 1.8, Information relating to Pharmacovigilance

12 DOCUMENT HISTORY

Version #	Implementation Date	Reasons for Change:
1	10 December 2021	New document