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MCA Technical Working Group

Guideline for Safety Monitoring of Medicines (Pharmacovigilance) including Vaccines

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This guideline replaces version 1 dated 10 December 2021 of the 'MCA Guideline for Safety Monitoring of Medicines (Pharmacovigilance) including Vaccines'.

Version #	**Implementation Date**	**Reasons for Change:**
1	10 December 2021	New document
2	02 May 2025	Format changed to the current template; editorial changes; reliance included; role of MAH's representative changed; requirements for applicants of MA moved to respective guideline; emerging safety issues moved to a separate section and more detailed.

Comments should be provided by using the template (MCA-F-021/03) for Submission of Comments and sent to info@mca.gm.

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Guideline for Safety Monitoring of Medicines (Pharmacovigilance) including Vaccines

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Acknowledgements

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1 Introduction (background)

1.1. During the development of medicines including vaccines and biologicals they are extensively investigated in human participants in clinical trials before their marketing authorisation (registration) by a regulatory authority.

1.2. However, everything related to their safety and risks cannot be determined in this period due to limitations of clinical trials:

- the numbers of trial participants are less than patients of real practice;
- trial participants are selective and certain groups such as pregnant women, the elderly, children and patients with other disease and concomitant treatments are often excluded; and
- the duration of clinical trials is limited as compared to real practice.

1.3. When these new medicines are released into the market after authorisation, a large population is exposed and previously unknown, unexpected adverse reactions can occur.

1.4. Therefore, thorough safety monitoring of marketed medicines (Pharmacovigilance) by all stakeholders is required.

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

1.6. Marketing authorisation holders (MAHs), manufacturers and healthcare professionals are key stakeholders in the continuous safety monitoring of medicines marketed in The Gambia.

2 Legal basis

2.1. 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.

2.2. 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.

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

2.4. In accordance with the Regulations 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.

2.5. In accordance with the Regulations and MCA Reliance Policy, the Agency recognises regulatory decisions, reports including inspections and recommendations from other Medicines Regulatory Agencies and international bodies like the WHO including the Global Advisory Committee on Vaccine Safety (GACVS). MCA may rely on methods, tools, common processes, standards and templates developed for the safety monitoring by other national and international organisations and implement changes to the existing processes accordingly, if necessary.

3 Purpose and Scope

1.1. 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.

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

1.3. It applies to marketing authorisation holders (MAHs), their representatives, manufacturers and other pharmacovigilance stakeholders.

1.4. 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*.

4 Marketing Authorisation Holders (MAHs)

4.1 General Requirements

4.1.1. MAHs of medicines marketed in The Gambia should ensure to monitor constantly the risks of their medicines, have in place an appropriate pharmacovigilance system of safety monitoring, ensure that appropriate action can be taken when necessary and ensure to report the results of this monitoring to the Agency.

4.1.2. MAHs shall permanently and continuously have at their disposal a person who is responsible for Pharmacovigilance, referred to as Qualified Person for Pharmacovigilance (QPPV) as described in section 4.3.

4.1.3. MAHs not resident in The Gambia must have a local representative residing in The Gambia at their disposal. The Agency may accept a regional representative residing a West African country. Where no local representative is identified, the importer fulfills this obligation. For details on representatives of MAHs refer to the MCA *Guideline for Marketing Authorisation (Registration) of Medicines*.

4.1.4. MAHs 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.

4.1.5. MAHs should monitor pharmacovigilance data to determine whether there are any new risks, whether risks have changed or whether the risk-benefit balance of their medicines have changed and update the risk management system as applicable.

4.1.6. MAHs and representatives of MAHs of medicines marketed in The Gambia should:

- inform the Agency of any new or existing quality, safety or effectiveness concerns related to any medicine, including but not limited to adverse reactions;
- operate a risk management system for their medicines, monitor the outcome of risk minimisation measures and inform the Agency of any risk management activities;
- evaluate all information about their products, examine risk minimisation and prevention measures and, where necessary, take such measures immediately;

- should not make any pharmacovigilance information public in The Gambia without notifying the Agency and shall ensure that such information presented is not false or misleading (see also section 9).

4.2 Reporting Requirements

4.2.1. MAHs and representatives of MAHs of medicines marketed in The Gambia shall submit to the Agency Individual Case Safety Reports (ICSRs) on suspected serious adverse reactions to a medicine that occurred in The Gambia, whether expected or unexpected, immediately but not later than 15 calendar days. For details on reporting of ICSR refer to the MCA *Guideline for Reporting of Adverse Reactions to Medicines including Vaccines*.

4.2.2. They should further communicate any of the following information immediately but not later than within 15 calendar days to the Agency:

- additional relevant information for a previously reported SAR or information about a case initially classified as non-serious;
- 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;
- lack of prophylactic efficacy of vaccines which 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.

4.2.3. 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.

4.2.4. Non-adherence to the requirements of this guideline by the MAHs and representatives of MAHs may result in sanctions imposed by the Agency.

4.3 Qualified Person for Pharmacovigilance (QPPV)

4.3.1. 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 representative of the MAH shall serve as the employer of the QPPV. Each representative of the MAH may appoint one QPPV to cover all the relevant products for his/her business.

Qualifications of QPPV

4.3.2. The QPPV shall be a healthcare professional registered with the relevant statutory body in The Gambia and being formally trained in pharmacovigilance by MCA or an institution recognised by the Agency.

4.3.3. The person designated as QPPV shall be a healthcare professional with Bachelors in Medicine and Surgery, MD, B. Pharm, Pharm D, BSc. Nursing, or any other healthcare professional degree recognised by the Agency.

4.3.4. 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 the QPPV

4.3.5. The QPPV should act as a single pharmacovigilance contact point for the Agency and also as a contact point for pharmacovigilance inspections.

4.3.6. He/she should establish and maintain the MAH's pharmacovigilance system (see section 4.4).

4.3.7. In addition, the responsibilities of the QPPV shall include but not limited to the following:

- Having an overview of the medicines' safety profiles and any emerging safety concerns;
- Being aware of any conditions or obligations including post-authorisation safety studies as part of the marketing authorisation and other commitments relating to safety or the safe use of the product;
- Provide to the Agency all pharmacovigilance-related documents such as:
  - Adverse Reaction reports as Individual Case Safety Reports, where applicable (for details refer to the MCA *Guideline for Reporting of Adverse Reactions to Medicines including Vaccines*);
  - Periodic Safety Update Reports (PSURs) or Periodic Benefit-Risk Evaluation Reports (PBRER), as applicable (see section 6); and
  - Risk Management Plans, where applicable (see section 7);
- Ensure full and prompt response to any request from the Agency for the provision of additional information necessary for the evaluation of the benefits and risks of a medicine;
- Communicate to the Agency the preparation of regulatory actions in response to emerging safety concerns (e.g. variations, urgent safety restrictions, recalls);
- 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 correctly, promptly and fully.

4.4 Requirements regarding the Pharmacovigilance System

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

4.4.2. The MAH should audit its pharmacovigilance system regularly at appropriate intervals, make a note of the important findings in its PSMF and ensure that corrective measures are taken to remedy deficiencies before the note is deleted from the file.

4.4.3. The PSMF should be permanently available for inspection and a copy should be provided within seven (7) days to the Agency, if requested.

4.4.4. 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.

4.4.5. The content of the PSMF should reflect global availability of safety information for medicines authorised in The Gambia, presenting information on the pharmacovigilance system applied at global, regional and local levels.

5 Medicines Control Agency (MCA)

5.1. With the aim to fully assess the benefit/risk profile of a medicine the Agency may ask the MAHs or representatives of MAHs to provide additional data on safety, efficacy or quality of medicines marketed in The Gambia, if it is necessary from a public health perspective.

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

- A Pharmacovigilance system plan.
- Pharmacovigilance activity to be listed in the RMP (non-clinical studies, clinical trials or non-interventional PASS/PAES) which are required to investigate a safety concern of a medicine 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 marketing authorisations (MA) 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)). For details on signals refer to the MCA Guideline for Signal Management.

5.3. 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.

5.4. MCA shall be responsible for the review, categorisation and follow-up of all reports and any other safety information of medicines received.

5.5. 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;
- monitor the outcome of risk minimisation measures contained in risk management plans,
- 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.

5.6. The Agency shall acknowledge the receipt of PSURs or PBRERs and communicate preliminary evaluation comments to the MAHs and representatives of MAHs within 28 calendar days of receipt of the report.

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

5.8. 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.

5.9. 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*.

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

5.11. The Agency shall cooperate with the World Health Organization (WHO) 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.

6 Periodic Safety Update Report (PSUR)/Periodic Benefit-Risk Evaluation Report (PBRER)

6.1. 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.

6.2. The main purpose of the PSUR/PBRER is the retrospective, integrated, post-authorisation risk-benefit assessment.

6.3. MAHs of both innovator and generic medicines and representatives of MAHs are required to submit PSURs or PBRERs to the Agency.

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

6.5. 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.

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

6.7. The recommendations as laid down in the European Medicines Agency (EMA) Guideline on good pharmacovigilance practices (GVP) Module VII – Periodic safety update report and of the ICH harmonised tripartite guideline, periodic benefit-risk evaluation report should be taken into consideration.

6.8. 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.

6.9. 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.

6.10. 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).

6.11. 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.

7 Risk Management Plan

For more details on the risk management system refer to the European Medicines Agency (EMA) guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems.

7.1. 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 authorisation to provide more information on the medicine's safety profile.

7.2. The main purpose of the RMP is the prospective pre-and post-authorisation risk-benefit management and planning.

7.3. 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.

7.4. 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.

7.5. 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

7.6. The RMP consists of seven parts as listed below; Part II, the Safety specification is 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/PBRERs). 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

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

7.8. If the RMP is submitted as part of the marketing authorisation (registration) 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.

7.9. 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.

7.10. 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.

7.11. 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 (see MCA *Guideline for Marketing Authorisation (Registration) of Medicines*).

8 Post-Authorisation Safety and Efficacy Studies

8.1. 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 requested by the Agency to be conducted by the MAH. A PASS or PAES may be interventional or non-interventional.

8.2. The recommendations as laid down in the European Medicines Agency (EMA) guideline on good pharmacovigilance practices (GVP) Module VIII – Post-authorisation safety studies and the EMA scientific guidance on post-authorisation efficacy studies should be taken into consideration.

8.3. 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

8.4. 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.

8.5. 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.

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

8.7. Whether conducted voluntarily or required by the Agency, the MAHs are responsible for the financing and conduct of PASS or PAES in The Gambia.

8.8. The requirements for clinical trials and observational Phase IV clinical studies, where applicable, as stipuletaed in the MCA *Guideline for Clinical Trials in Humans* apply.

8.9. With respect to adverse reactions occuring during the study, the MCA *Guideline for Reporting of Adverse Reactions to Medicines* applies, unless the Agency specifies different requirements for the PASS or PAES.

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

8.11. MAHs 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.

9 Safety Communication

9.1. Throughout the life cycle of the medicine 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 take or use or prescribe, handle, dispense or administer the medicines.

9.2. 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; and
- support public confidence in the regulatory system.

9.3. 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.

9.4. Safety Communication issued by MAHs residing in The Gambia or specifically addressed to the Gambian population by the MAHs or representatives of MAHs 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).

9.5. Types of Safety Communication can be as follows:

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

9.6. 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 MAH and the Agency on the safety information provided;
- information on proposed change to the product information (e.g. the summary of product characteristics (SmPC) or package information leaflet (PIL) as stipulated in the MCA *Guideline for Variation*;
- 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 Medicines including Vaccines*.

10 Safety Monitoring during Public Health Emergency

10.1. 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.

10.2. 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.

10.3. Emergency Use Authorisation (EUA) procedure will be realised in accordance with the national requirements and in accordance with the MCA *Guideline for Emergency Use Authorisation of Medicines*. A risk-benefit approach will be used for assessing and listing unapproved 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.

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.

10.4. All adverse reactions (ARs) and AEFIs 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 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 should be followed up accordingly.

10.5. 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.

10.6. 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.

10.7. Reporting forms will be distributed to all relevant health facilities recognised by the Ministry of Health.

10.8. 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.

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

10.10. AR and AEFI reports will be submitted to the MSEC for review. The assessment of these AR 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.

11 Emerging Safety Issue (ESI)

For more details on Emerging Safety Issues refer to the European Medicines Agency (EMA) guideline on good pharmacovigilance practices (GVP), Module IX – Signal management.

11.1. An emerging safety issue (ESI) is defined as a safety issue considered by a MAH to require urgent attention by the authority because of the potential major impact on the risk-benefit balance of the medicine and/or on patients' or public health, and the potential need for prompt regulatory action and communication to patients and healthcare professionals.

11.2. Examples include:

- major safety issues identified in the context of ongoing or newly completed studies, e.g. an unexpectedly increased rate of fatal or life-threatening adverse events;
- major safety issues identified through spontaneous reporting or published in the scientific literature, which may lead to considering a contra-indication, a restriction of use of the medicine or its withdrawal from the market;
- major safety-related regulatory actions e.g. a restriction of the use of the medicine or its suspension.

11.3. When MAHs become aware of an ESI from any source, they should notify it in writing to the Agency by email to info@mca.gm. This should be done as soon as possible and no later than three (3) calendar days after establishing that a

validated signal or a safety issue from any source meets the definition of an emerging safety issue.

11.4. When notifying an ESI, the MAH should describe the safety issue, the source(s) of information, any planned or taken actions with timelines (e.g. temporary or permanent cessation or suspension of marketing of a medicine, withdrawal of a medicine from the market, request for the withdrawal of a marketing authorisation or non-application for the renewal of a marketing authorisation), and should provide any relevant documentation available at the time of initial notification. Any further information relevant to the issue should be provided to the Agency as soon as it becomes available.

11.5. Upon being notified of an ESI, the MCA will promptly assess the urgency and potential impact of the issue and agree on appropriate next steps and the potential regulatory procedure to address the matter raised.

11.6. The MAH should collaborate with the Agency in the assessment of the ESI. The MAH should only communicate as ESI those safety concerns which meet the definition provided above and whose urgency and seriousness cannot permit any delay in handling.

12 Additional Measures

12.1. Training for healthcare professionals on the use of the recommended medicines, medicines safety aspects and reporting of ARs will be provided by MCA. Refer to the MCA *Guideline for the National Pharmacovigilance System*.

12.2. 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.

12.3. 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*.

12.4. Interactions with international partners, regulatory and public health authorities and agencies are constantly 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 and reliance measures respecting confidentiality agreements.

Definitions

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

The definitions provided below apply to the terms used in this guideline. They may have different meanings in other contexts and documents.

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-authorisation 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.

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.

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

Post Authorisation Efficacy Study (PAES)
Any study conducted within the authorised therapeutic indication to address well-reasoned scientific uncertainties on aspects of the evidence of benefits that should be, or can only be, addressed post-authorisation.

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 to the Agency by a patient, consumer, healthcare professional, marketing authorisation holder, representative of a MAH or any other organisation 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.

References

- Medicines and Related Products Act, 2014
- Medicines and Related Products Regulations, 2020
- MCA Guideline for Marketing Authorisation (Registration) of Medicines (MCA-GL-102)
- MCA Guideline for Reporting of Adverse Reactions to Medicines including Vaccines (MCA-GL-305)

- MCA Guideline for Signal Management (MCA-GL-309)
- MCA Guideline for Clinical Trials in Humans (MCA-GL-501)
- MCA Guideline for Variation (MCA-GL-114)
- MCA Guideline for Emergency Use Authorisation of Medicines (MCA-GL-120)
- MCA Guideline for the National Pharmacovigilance System (MCA-GL-308)
- WAHO Good Pharmacovigilance Practice Guidelines, 2018
- ICH Harmonised Tripartite Guideline. Pharmacovigilance Planning (E2E). 18 November 2004
- ICH Harmonised Tripartite Guideline. Periodic Benefit-Risk Evaluation Report (PBRER) E2C(R2). 17 December 2012
- EMA. Guideline on good pharmacovigilance practices (GVP) Module VII – Periodic safety update report (EMA/816292/2011 Rev 1). 9 December 2013
- EMA. Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (EMA/838713/2011 Rev 2). 28 March 2017
- EMA. Guideline on good pharmacovigilance practices (GVP) Module VIII – Post-authorisation safety studies (EMA/813938/2011 Rev 3). 9 October 2017
- EMA. Guideline on good pharmacovigilance practices (GVP) Module IX - Signal management (EMA/827661/2011 Rev 1). 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

Flow Chart: Management of Side Effects