بسم الله الرحمن الرحيم

Maldives Food and Drug Authority

Ministry of Health

Male', Maldives

Guideline on Pharmacovigilance and ADR Reporting

Guideline on Pharmacovigilance and ADR Reporting is released under the authority of

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It is the property of:
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Guideline on Pharmacovigilance and ADR Reporting

1 INTRODUCTION

As more pharmaceutical products come on the market and more people gain access to those products, it has become imperative for countries to monitor the safety of medicines and protect the public from medicine-related harm. Pharmacovigilance plays a key role in ensuring that medicines are safe for patients by assessing, monitoring, and identifying effects and interactions of drugs.

What is Pharmacovigilance?

Pharmacovigilance (PV) is the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problem. Recently, the definition of Pharmacovigilance has been expanded to include problems related to any pharmaceutical product, including vaccines, medical devices, biologics, blood products, herbal medicines and traditional and complementary medicines. Pharmacovigilance promotes public health by ensuring the safety, efficacy, and quality of medicines, and other health products.

2 PURPOSE

This guideline briefly highlights the Pharmacovigilance system in relation to Adverse Drug Reaction (ADR) reporting and Adverse Drug Events (ADE) reporting in the Maldives, and outlines what, why, when, where, and how to report ADRs and ADEs and information on the safety, efficacy, and quality of pharmaceuticals and other health products.

3 SCOPE

The PV system is focused on detecting, evaluating, and preventing Adverse Drug Events(ADE) related to medicines and other pharmaceutical products by managing and mitigating the risk that such products pose to patients. ADE reporting emphasizes reporting on medication errors as well as product quality issues.

The medicines and other health products monitored by the PV system include:

- Conventional (allopathic)
- Medicines/Vaccines
- Medical devices
- Biological
- Blood products
- Alternative Medicines (e.g., Ayurvedic, Unani, Herbal, Homeopathic, Biochemical)

4 Definitions:

4.1 Adverse Drug Events (ADE):

An Adverse Drug Event or ADE is defined as, any untoward medical occurrence that may occur during treatment with a pharmaceutical product but that does not necessarily have a causal relationship with this treatment. Adverse Drug Events are directly related to pharmaceutical products and may be due to:

- Known or unknown pharmacological properties resulting in ADRs
- Poor product quality (e.g., spurious, adulterated, misbranded, counterfeit, substandard)
- Medication errors in prescribing, preparing, administering, or taking the medicine

4.2 Adverse Drug Reactions:

An ADR is a response to a drug that is harmful and unintended and occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of a disease, or for the modification of physiological function.

An unexpected adverse reaction is an adverse reaction for which the nature or severity is not consistent with the labelling or market authorization or expected from characteristics of the drug. An ADR is distinct from an ADE in that ADR is harm directly caused by the drug at normal doses, during normal use.

5 What is the aim of pharmacovigilance?

Pharmacovigilance is aimed at:

- Monitoring and detecting medicine safety, effectiveness, and quality problems through passive and active surveillance of adverse events.
- Assessing the safety, quality, effectiveness, and risk/benefit of pharmaceutical products
- Disseminating information on the safety and appropriate use of pharmaceutical products to the

public and health care professionals to mitigate risk.

- Monitoring and engaging pharmaceutical importers and other stakeholders to ensure that marketed drugs are of high quality and are safe for human consumption.

6 Pharmacovigilance in the Maldives

6.1 PIDM

6.1.1 In 2016, Maldives received the full membership of The WHO Programme for International Drug Monitoring (PIDM) and became the 125th member of the program. PIDM is a forum for collaboration between member states in the monitoring of drug safety and analysis of Adverse Drug Reactions (ADR).

6.1.2 To participate in the WHO Program for International Drug Monitoring, MTG collaborates with WHO-UMC (Uppsala Monitoring Centre). A range of software tools (VigiFlow, VigiBase, VigiSearch, VigiMine, VigiMed, VigiLyze) are provided by WHO-UMC to achieve the objectives of the PV program in a more efficient way.

6.1.3 Medicine and Therapeutic Goods division (MTG) of Maldives Food and Drug Authority (MFDA) is responsible for the monitoring, reporting and implementation of PV in the country. It serves as the coordinating body for the national PV system in the country; Collaboration with WHO-UMC.

6.2 MFDA/MTG's role

6.2.1 The key responsibilities of MTG (PV Monitoring Section) include:

- Reviewing, evaluating, and analysing Adverse Drug Events (ADE) reports, including serious ADE reports, and making recommendations on appropriate regulatory actions and effective ways of communicating information on medicine safety to health care professionals, and the public;
- Assessing pharmaceutical risks and making recommendations in this regard;
- Implementation of the PV program and approaches on how to promote the safe and effective use of medicines by Health Care Professionals and the public
- Reviewing mechanisms for collecting and improvement strategies for ADEs in the country

- Develop and implement risk minimisation strategies to address drug safety concerns

6.3 Who are the other stakeholders and what are they responsible for?

6.3.1 The effectiveness of the national PV system depends on the participation of all actors within the system and their fulfilment of the roles and responsibilities. There are a number of stakeholders in pharmacovigilance with different roles and responsibilities. They include the following.

- **Ministry of Health:**
  - collaboration and coordination in reporting, policy making, and decision making.
  - Financial support on sustaining PV program and PIDM membership.
- **All hospitals and Health facilities in the country:**
  - Appoint a PV focal point from each hospital
  - Train health care professionals within their respective hospitals on how to recognise and report on adverse events
  - Collect all Adverse Drug Reaction Reporting Form from health care professionals in the facility and ensure that these are filled out accurately and completely
  - Submit ADE reports to the MFDA, MTG as per the standard reporting procedure
  - Ensure that all ADE reports are kept confidential and that the identities of patients and reporters and the trade names of the suspected drug are not disclosed
  - Take corrective action, as appropriate, in consultation with health care facilities
  - Implement recommendations from the MFDA, MTG to mitigate risk and prevent adverse events
  - Promote rational use of medicines and other health products.
- **Pharmacies:** reporting ADEs and ADRs reported by customers.
- **Public health programs in the Maldives:** Public Health Programs shall collaborate and coordinate closely with the MTG on PV activities. MTG will establish a letter of agreement/Memorandum of Understanding with respect to the collection and processing of ADE reports generated and collected through the health program. In addition, health programs shall
  - set research priorities for active surveillance studies based on the products used in their programs and specific safety concerns.

- Train health workers in the appropriate use of the pharmaceutical products in their programs treatment guidelines and adverse event reporting.

- **Health care professionals (e.g., doctors, pharmacists, nurses) and professional associations:**
  - Detect and appropriately manage adverse events associated with the use of medicines.
  - Document and immediately report all serious and non-serious suspected adverse events, including unknown or unexpected ADRs, unexpected therapeutic effects, all suspected drug interactions, product quality problems, treatment failures, and medication errors.
  - Advise patients on drug interactions and possible ADRs.
  - Prevent the occurrence of medication errors and other avoidable adverse events by using medicines rationally.
  - Implement a mechanism to communicate reported ADRs with stakeholders (doctors, nurses).
  - Establish a mechanism for reporting ADR at peripheral level, identify focal points and providing access.
  - Conduct training for doctors and focal points on reporting ADR and promote ADR reporting.
- **Retailers/ community pharmacist's/ pharmacist assistants:**
  - Fill out an Adverse Drug Reaction Reporting Form when patients/consumers report a suspected adverse drug event
  - Immediately report any suspected ADRs, drug interactions, unusual effects, or product quality concerns to the MFDA, MTG by submitting the Adverse Drug Reaction Reporting Form
  - Advise patients on possible ADRs and drug interactions at the time of dispensing based on the most current information available

Doctors and nurses report ADR through focal points

- **Patients/ consumers:** Report any adverse event that may be associated with the use of pharmaceutical products immediately to their health care provider or directly to MFDA, MTG using the standard Adverse Drug Reaction Reporting Form (Annex 1).

- **Media:** Reporting information regarding ADEs and ADRs, facilitate communication regarding product safety and usage.
- **PV centres in other countries:** collaborating, coordinating, and informing the PV centres in other countries regarding ADEs and ADRs reported locally through updating and reporting to the established databases of WHO.
- **Pharmaceutical Marketing Authorization Holders and Pharmacies**
    - Inform MFDA, MTG of any serious ADR arising from the use of a products immediately and no later than one week after the reporting of such adverse reactions
    - Ensure that an appropriate PV reporting system is in place within the company to accept responsibility and liability for the product marketed
    - All pharmaceutical Marketing Authorization Holders shall provide periodic safety update reports of registered products to MFDA /MTG when required
    - Respond promptly and fully to requests for risk/benefit information from MFDA, MTG
- **WHO/ UMC (Uppsala Monitoring Centre):**
    - Receive and store ADE reports from the MFDA, MTG in VigiBase (database)
    - Provide guidance, technical support, and training for MFDA, MTG staff
    - Provide tools, trainings, and access to information systems to enable the MFDA, MTG to search the global WHO database
    - Monitor signals from the global WHO database (a signal refers to reported information on a possible causal relationship between an adverse event and a drug when the relationship is unknown or documentation is incomplete)
    - Facilitate communication among countries
    - Provide regular feedback and specific services on request

6.4 Who Can Report?

6.4.1 All health care professionals, including doctors, nurses, and pharmacists, community health workers, patients, consumers, and the public can report ADEs and ADRs.

6.5 What to Report?

6.5.1 All suspected adverse events and related information (as indicated in the Adverse Drug Reaction Reporting Form) should be reported through the appropriate channels.

6.5.2 Suspected Adverse Drug Events include all events related to:

- ADRs (severe and non-severe)
- Product quality
- Medication errors
- Therapeutic ineffectiveness
- Abuse

6.5.3 Suspected product quality issues, which may or may not have resulted in an observable or reported adverse event, include all products that show signs of:

- Discolouration or colour change
- Separation of components
- Powdering/crumbling
- Caking
- Moulding
- Changes in smell
- Poor packaging
- Poor labelling or mislabelling
- Suspected contamination
- Questionable stability
- Defective components
- Suspected Counterfeit

6.6 Reporting AEFI (Adverse Event Following Immunization)

6.6.1 Immunization is one of the most effective public health interventions to protect individuals and the public from vaccine-preventive diseases and has saved millions of lives. Modern vaccines are safe and effectively protect individuals and public. However, vaccines like other medicinal products are not free from occasional adverse reactions.

6.6.2 An adverse event following immunization (AEFI) can range from mild to rare and serious. Vaccines

rarely cause serious adverse reactions, and common reactions are minor and self-limited. In the majority of serious cases, these are merely coincidental and have no relationship to the vaccine. In others, they are caused by an error in transportation, storage, preparation, or administration of the vaccine.

6.6.3 National immunization program focal point should send all AEFI reports to National Pharmacovigilance program, that's run by MTG's PV section.

6.7 When to Report?

6.7.1 Serious adverse drug events (those that result in death, life-threatening conditions, disability, congenital anomaly, hospitalisation, or modification of therapy due to toxicity) should be reported to the MTG's PV section, or PV focal point where available, as soon as they occur or the reporter is notified of them. All PV focal points are required to submit completed ADR reporting forms to PV section of MTG. The reporting form for serious adverse events (Adverse Drug Reaction Reporting Form) must be filled and sent to MTG within 24 to 48 hours.

6.7.2 Non-serious adverse event reports should be submitted to the MTG's PV section no later than one week after they were reported to the health facility.

6.7.3 Poor product quality issues should be reported as soon as possible, following the same scheme as that for adverse events.

6.8 How to report?

6.8.1 Patients should report any unexpected deterioration in physical, chemical, or neurological status following the use of a medicine or other health product and any quality concerns about a product to a healthcare professional at a health facility. The provider or facility can properly examine the product, collect all relevant information, and take prompt action to ensure the patient's safety and well-being.

6.8.2 If a patient/consumer does not have immediate access to a healthcare professional or a health facility, he or she can report to a community health worker or directly to the MTG

pharmacovigilance section

6.8.3 Healthcare professionals should fill out the ADR Reporting Form for any suspected adverse event or suspected product quality issue and submit it to the PV focal point at their facility.

6.8.4 If a facility does not have a designated Pharmacovigilance focal point or other appointee to receive Adverse Drug Reaction Reporting Forms, the Healthcare professionals at that facility can report directly to the PV section of MTG.

6.8.5 PV focal points should collect all forms and submit the forms to the PV section of MTG.

6.8.6 ADE reports can be submitted to MTG by email (mtg@health.gov.mv), or fax. In emergency cases and when forms are not available, events can also be reported to MTG by phone (3014316/ 3014322). In some cases, for example, if it is considered an emergency situation or forms are not readily available a reporter can also contact PV section of MTG directly by phone or email to inform them about an adverse event. PV section will then complete an Adverse Drug Reaction Reporting Form on the reporter's behalf. Reporters are encouraged to collect and report all available information on the adverse event when they contact the MTG'S PV section.

6.8.7 The minimum information required is:

- Current medication
- Suspected adverse event information
- Product information
- Contact information for the reporter

6.8.8 All reported information will remain confidential. The name, designation, age, gender, and addresses of both the patient and the physician will not be disclosed.

6.8.9 The submission of spontaneous reports of suspected adverse events should be guided by:

- Prompt reporting
- Immediately reporting of any suspected ADR
- Accuracy and completeness: Completing each Adverse Drug Reaction Reporting Form accurately and legibly and including as much information as can be collected about the patient (comorbidities and current medication), the event, and the product. All of the information

requested on the form is important for the causality assessment.

6.9 What are the benefits of prompt reporting?

6.9.1 Public, health professionals, and patients benefit from the reporting of ADRs and ADEs in many ways it can:

- Improve quality of care offered to patients
- Reduce medicine-related problems and better treatment outcomes
- Improve patient confidence in professional practice and potential for increased use of professional health care services
- Improve access to information on medicine-related problems reported within the country and internationally
- Provide satisfaction in fulfilling a moral and professional obligation

6.10 What actions are taken by MFDA following a ADR/ADE report?

6.10.1 When MTG'S PV section receives an adverse event report, the report is processed according to the following steps:

6.10.1.1 A unique identification number will be assigned to the form.

6.10.1.2 The form will be reviewed to ensure that all necessary information is included; if any information is incomplete, the responsible officer will communicate directly with the report sender to obtain any the missing information/ additional information/ documents are required.

6.10.1.3 Perform causality assessment by using Naranjo scale (Annex 2).

6.10.1.4 Evaluate and investigate serious adverse events (e.g., death) (or conduct joint inspection and collaborate with Ministry of Health's Quality Assurance team if required) and prepare a case history as soon as possible. It will be then submitted to PV team or National Pharmaceutical Board for review and assessment.

6.10.2 Before taking the necessary regulatory measures MFDA, MTG will seek advice from Ministry of Health's policy level and National Pharmaceutical Board.

6.10.3 Confirmed adverse events may result in the following actions:

- Additional investigations into the use of the product
- Changes to the package and product information
- Changes in the recommended use of the pharmaceutical product
- Educational initiatives to improve the safe use of the product
- Other regulatory and health promotion interventions that may be warranted, including product withdrawal/recall/suspension from market

6.10.4 The outcome of the notified adverse event will also be communicated directly to the healthcare professional and facility which reported the case. In addition, MFDA, MTG will communicate any potential risks to the public and health care facilities through the media, newsletters, and other channels.

7 Reference documents:

- Medicine Regulation 2014/R-46

8 Annexes

- Annex 01: Adverse Drug Reaction Reporting Form
- Annex 02: Naranjo Causality Scale (a Naranjo Causality Scale (adapted))

Contact

- Hotline Number: 7200321
- E-mail: mtg@health.gov.mv

Annex 01: Adverse Drug Reaction Reporting Form

Adverse Drug Reaction Reporting Form

Report No.: Maldives Food and Drug Authority
Ministry of Health
Male', Maldives

Report No.:

*Fields marked * are MANDATORY information to be completed and provide as much detail as possible for all other fields. Information provided in this form will remain confidential. Please attach additional sheets as required.*

Patient Details

Name/ Initials: Hospital no./Record no.

*Date of Birth: OR Age at onset: *Sex: M / F

Weight: Height: *Date of death(if applicable): *Cause of death(if applicable):

*Medical History (Pregnancy, allergies, renal/hepatic function and other diseases etc.):

Relevant investigations done:

Reporter Information

Name:

Address of Institute: Designation:

Contact Number:

Email:

Profession: ☐ Physician ☐ Pharmacist ☐ Other Health Professional ☐ Consumer/non health professional

Date:

Signature:

***Adverse Reaction/ Event Details**

Date of start of reaction: Time of onset of reaction: Date reaction ended:

Reaction subsided after stopping the drug/reducing the dose: ☐ Yes ☐ No ☐ Unknown ☐ N/A(drug continued)

Reaction reappeared after restarting the drug: ☐ Yes ☐ No ☐ Unknown ☐ N/A(drug continued)

Seriousness of reaction: ☐ Life threatening ☐ Caused/prolonged hospitalization ☐ Caused disability ☐ Resulted in congenital anomaly ☐ Other medical condition ☐ N/A

Outcome of reaction: ☐ Recovered ☐ Recovering ☐ Not ☐ Recovered ☐ Unknown ☐ Fatal

Relatedness of drug to reaction: ☐ Certain ☐ Probable ☐ Possible ☐ Unlikely ☐ Conditional ☐ Unassessable

Reporter's brief on event:

***Suspected Drug (s)**

Drug Name (Brand name)	Batch No.	Dosage & duration	Route of admin.	Indication	Date started	Date Stopped	Action taken

***Concomitant Drug(s)**

Drug Name (Brand name)	Batch No.	Dosage & duration	Route of admin.	Indication	Date started	Date Stopped	Action taken

Thank you for reporting.

Annex 02: Naranjo Causality Scale (a Naranjo Causality Scale (adapted) [1]

1. Are there previous conclusive reports on this reaction?

   Yes (+1) **No (0)** **Do not know or not done (0)**

2. Did the adverse event appear after the suspected drug was given?

   Yes (+2) **No (-1)** **Do not know or not done (0)**

3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?

   Yes (+1) **No (0)** **Do not know or not done (0)**

4. Did the adverse reaction appear when the drug was re-administered?

   Yes (+2) **No (-1)** **Do not know or not done (0)**

5. Are there alternative causes that could have caused the reaction?

   Yes (-1) **No (+2)** **Do not know or not done (0)**

6. Did the reaction reappear when a placebo was given?

   Yes (-1) **No (+1)** **Do not know or not done (0)**

7. Was the drug detected in any body fluid in toxic concentrations?

   Yes (+1) **No (0)** **Do not know or not done (0)**

8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?

   Yes (+1) **No (0)** **Do not know or not done (0)**

9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?

   Yes (+1) **No (0)** **Do not know or not done (0)**

Scoring

- **> 9 = definite ADR**
- **5-8 = probable ADR**
- **1-4 = possible ADR**
- **0 = doubtful ADR**

[1] Naranjo et.al. "A method for estimating the probability of adverse drug reactions." *Clinical Pharmacology & Therapeutics*. 1981 Aug;30(2):239-45