بسم الله الرحمن الرحيم

Maldives Food and Drug Authority

Ministry of Health

Male', Maldives

Guideline on Pharmacovigilance and ADR Reporting

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Ms.Thooma Adam

Deputy Director General

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Prepared by:
Director, Pharmaceuticals
Aishath Jaleela

Approved by: **Ms.Aishath Mohamed** **Deputy Director General, Pharmaceuticals** **Maldives Food and Drug Authority**		23.06.2022
Authorised by: **Ms.Thooma Adam** **Deputy Director General, Laboratory Services** **Maldives Food and Drug Authority**		23.06.2022

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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.

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 highlights the Pharmacovigilance system in relation to Adverse Drug Reaction (ADR) reporting in the Maldives, and outlines what, why, when, where, and how to report ADRs 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 Reactions (ADR) related to medicines and other pharmaceutical products by managing and mitigating the risk that such products pose to patients. ADR reporting emphasizes reporting on medication errors as well as product quality issues in related with efficacy .

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

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

4 Guideline Content

4.1 Pharmacovigilance in the Maldives

4.1.1 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).

4.1.2 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.

4.1.3 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.

4.2 Responsibilities and Accountability

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**.**

MFDA/MTG Enforcement

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

- MTG enforcement Section is responsible to conduct and coordinate all the vigilance activities
- Reviewing, evaluating, and analysing Adverse Drug Events (ADE) reports, including serious ADE reports,
- Implementation of appropriate regulatory actions
- effective communication and sharing of 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
- Conduct awareness for MAHS, Health professionals and to the public.
- Identify PV focal points from Health facilities and coordinate with them.
- 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)
- Maintain confidentiality and promote transparency and accountability of the PV team .
- Provide regular feedback on the submitted reports

National Pharmaceutical board

- Verification of Causality assessment performed by Enforcement Section.
- Provide recommendations on appropriate regulatory actions.
- Assessing pharmaceutical risks and making recommendations in this regard

Healthcare Professionals

- HCPs working in healthcare facilities are the main source of information in pharmacovigilance. This includes all prescribers, pharmacists, pharmacy technicians, dentists, midwives, nurses and other.
- 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 (Guideline for Quality Defects and Product Recall MTG/QA-DR/GLN-TE 004) , 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.

healthcare providers at all levels of a healthcare facilities can directly report to MTG or they can

report through the PV focal points identified by the hospital management

Market Authorisation Holders (MAHS)

Pharmaceutical manufacturers being primarily responsible for the safety of their products, on behalf of the Manufacture MAHs shall ensure that they campaign for and work closely with the HCPs to collect the suspected adverse reactions to their products and reported to MTG.

- All MAHs must establish an appropriate system of pharmacovigilance (PV) in the company. This is a way the company demonstrates that it accepts responsibility and liability for its products on the market and their safe use.
- Receive and store the records of ADE reports ,
- Develop a risk minimizing Plan and should be communicated with MTG
- Continuously monitor the safety of their products in the market is the prime responsibility of the MAHS.
- appoint a PV focal point and it should be communicated with MTG
- provide periodic safety update (As per product registration guideline) reports of registered products to MFDA /MTG when required
- Foreign ICSRs (ADRs occurring outside Maldives) should NOT be forwarded to MTG on a routine basis but should be reported in the context of a specific safety issue or on request by MTG. MTG should be advised of any emerging safety issue or action, which has been taken by any foreign agency, including the basis for such an action, within 5 calendar days of first knowledge by MAH. Safety related withdrawal/suspension of the registration status in any country should also be notified within 48-72 HOURS of first knowledge by the MAH

Ministry of Health:

- collaboration and coordination with Government hospital
- 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
- Coordinate with MTG to conduct training for new recruited Doctors and Nurses and ensure that the training is continuous.

- 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
- 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
- Implement recommendations from the MFDA, MTG to mitigate risk and prevent adverse events
- Promote rational use of medicines and other health products.

Pharmacies

- 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

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.

Patients/ consumers:

- Patients /Consumers are the key personal of the PV program

- All Patients are advice to 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).

Risk Management Plan

All MAHs required to submit a risk management plan of the company. The RMP should include the following criteria:

- Objectives of the risk minimization
- Routine risk minimization activities
- Additional risk minimization activities if any, individual objectives and justification of why needed
- How the effectiveness of each risk minimization activities will be evaluated in terms of attainment of their stated objectives
- What the target is for risk minimization i.e. what are the criteria for judging success, milestones evaluation and reporting.

5 Guideline Content

5.1 Who Can Report?

5.1.1 All health care professionals, including doctors, nurses, and pharmacists, community health workers, patients, consumers, hospital PV focal points and the public can report ADEs and ADRs.

5.2 What to Report?

5.2.1 All suspected adverse events and related information (as indicated in the Adverse Drug Reaction Reporting Form annex 1) should be reported through the appropriate channels. The form is available at Dhiriti Portal

5.2.2 Reporters are encouraged to report the following;

5.2.2.1 **All Suspected Adverse Reactions** - whether known or unknown, serious or nonserious, mild, moderate or severe reactions. This includes ADRs due to medication errors, and accidental or intentional drug overdose.

5.2.2.2 **Lack of Efficacy –** Including antimicrobial resistance and treatment failures.

5.2.2.3 **Suspected Pharmaceutical Defect (Quality defect)** - If an adverse event is suspected to be related to a product defect, it should be reported in the same manner as a suspected adverse reaction. The lot number of the suspected medicine should be included in the report, if available.

Other quality defects without Adverse event should be reported as per the Guideline for Quality Defects and Product Recall (MTG/QA-DR/GLN-TE 004)

5.2.2.4 **Drug Interactions** - Any drug- drug and drug-food interaction which results in an adverse outcome or lack of desired effect should be reported as an adverse reaction in the prescribed manner.

5.2.2.5 **Over Dosage** - Reports of overdose should be submitted only when an adverse reaction was associated with such an overdose, either intentional or accidental.

5.3 Reporting AEFI (Adverse Event Following Immunization)

5.3.1 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.

5.3.2 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.

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

5.4 When to Report?

5.4.1 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 hotline , 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 annex 1) must be filled and sent to MTG within 24 to 48 hours.

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

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

5.5 How to report?

5.5.1 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.

5.5.2 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

5.5.3 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.

5.5.4 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.

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

5.5.6 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 (7200321 / 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.

5.5.7 The minimum information required is:

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

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

5.5.9 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.

5.6 Completing the ADR reporting form

5.6.1 The ADR reporting form contains key data elements about the patient, the suspected drug, the adverse reaction, the action taken and the outcome . Such elements enhance the quality of an ADR report. Reporters should write legibly and use a separate form for each patient. Attempts should be made to obtain as many information as provided below:

5.6.1.1 The patient's identity – Information about the patient's age, sex, weight and other health conditions should be identified. The patient file number has to be stated as it is useful to get additional information when needed.

5.6.1.2 Information on the suspected drug –

- This information includes the name of the medicine, source, the dose, route of administration and the impact of withdrawal and re-administration of the suspected medicine on the adverse reaction. Use brand name of suspected medicine(s). If generic name is used, specify the manufacturer of the medicine. Avoid non-standard abbreviations such as TCL (tetracycline), PCM (Paracetamol), CPZ (Chlorpromazine), etc. List any other prescription, non-prescription medicines and/or traditional medicine used concurrently with the suspected medicine with all descriptions i.e. brand name, route, dosage form, strength, frequency, indication, date started and date stopped.
- The dosage form such as tablet, capsule, syrup, suspension, elixir, emulsion, injection, eye drop/ointment, topical crème/ ointment, nasal drop, suppositories rectal/ vaginal etc. should be stated. The strength must also be expressed in metric system, e.g. 500mg tab, 250mg/5ml syrup, 1gm rectal suppository etc. Sometimes strength can be expressed in %, e.g. 2% hydrocortisone ointment. Frequency of drug administration should be clearly notified using standard abbreviations, e.g. 3 times a day as tid or 8hrly, 2 times a day as bid or 12hrly, 4 times a day as qid or 6 hrly etc. Route of administration expressed using standard abbreviation should be used .
- The date medicine was started and discontinued (if applicable) is important data to assess the cause and effect relationship of the medicine and adverse reaction. Therefore

it has to be stated clearly on the reporting form as date/ month/year. If the medicine has not been discontinued at the time of reporting, write continuing. Write the reason why the medicine was used or the diagnosis for which the medicine was prescribed for both suspected medicine and other medicines used concurrently.

5.6.1.3 Additional information – Any reaction the patient may have experienced previously, particularly similar to the current adverse event, either caused by the same or different medicine has to be reported. Other relevant medical history, such as allergy, chronic disease, pregnancy and other factors shall also be included in the report

5.7 Follow-up report for an ADR that has already been reported –

5.7.1 Any follow-up information for an ADR that has already been reported can be sent on another ADR form, or it can be communicated by telephone, fax or e-mail to MTG indicating that it is a follow up information. The date of the original report and the report case number must be retrieved from the ADR register so that the follow up information can be matched with the original report. It is very important that follow-up reports are identified and linked to the original

5.8 Communicating with reporters and other stakeholders

5.8.1 Adverse reaction reports and other quality defect reporting forms sent to MTG should be acknowledged after receipt. Acknowledgement can be made via MTG official email within one (1) week, where possible. This will motivate and encourage reporters to keep sending reports and as a result improve the reporting rate.

5.8.2 Signals generated by running queries on Vigiflow should be communicated to health care providers and all other stakeholders. Results from the literature scan, statistics and regulatory measures taken should be communicated to health care providers and other stakeholders through MTG newsletters and MOH website and all other possible means

5.9 What are the benefits of prompt reporting?

5.9.1 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

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

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

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

5.10.1.2 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.

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

5.10.1.4 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.

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

5.10.3 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

5.10.4 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.

6 Reference documents:

- Medicine Regulation 2014/R-46

7 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