HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

September 2023

MEDICAL DEVICE GUIDANCE

GN-05: Guidance on the Reporting of Adverse Events for Medical Devices

Revision 3

HSA Health Sciences Authority

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PREFACE

R2.1 ►This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action/decision taken or not taken as a result of using this document. The information contained in this document should not be a substitute for professional advice from your own professional and healthcare advisors. ◄

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REVISION HISTORY

Guidance Version (Effective Date) *[3 latest revisions]*	Revision
GN-05: Revision 1 (October 2008)	R1
R2 ►GN-05: Revision 2 (September 2013)	R2
R2.1 ►GN-05: Revision 2.1 (01 November 2017)	R2.1
GN-05: Revision 2.1 (01 November 2022) – Reviewed: Remains valid	R2.1
R3 ►GN-05: Revision 3 (08 September 2023)	R3

**Where applicable, changes and updates made in each document revision are annotated with or within the arrow symbol "►". Deletions may not be shown.*

1. INTRODUCTION

1.1. Purpose

This document provides guidance on the requirements for reporting of adverse events (AE) for all medical devices.

1.2. Background

R3 ►The Authority uses a number of post-marketing risk assessment measures to ensure the continued safe use of medical devices. These measures include reporting from healthcare professionals, consumers or patients, mandatory reporting from medical device dealers, and exchange of regulatory information with other medical device regulatory agencies. ◄

The mandatory reporting of AEs by medical device dealers is an important part of the post-market surveillance system. The objective of AE reporting and subsequent evaluations is to improve protection of the health and safety of patients, users and others by disseminating information that may reduce the likelihood of, or prevent repetition of AEs, or alleviate consequences of such repetition.

The manufacturers, importers, suppliers and/or registrants are responsible for investigating adverse events involving medical devices they deal with and report their findings to the Authority. The Authority monitors adverse event investigations conducted by manufacturers, importers, suppliers and/or registrants of medical devices.

1.3. Scope

This document is applicable to all persons who register, manufacture, import and supply medical devices in Singapore. Persons who register, manufacture, import and supply medical devices in Singapore shall also be referred to as dealers of medical devices in this document.

1.4. Definitions

Definitions that do not indicate they are set out in the Health Products Act (*Act*) and Health Products (Medical Devices) Regulations 2010 (*Regulations*) are intended as guidance in this document. These definitions are not taken verbatim from the above legislation and should not be used in any legal context. These definitions are meant to provide guidance in layman terms.

ADVERSE EFFECT *(as set out in the Act)*: means any debilitating, harmful, toxic or detrimental effect that the medical device has been found to have or to be likely to have on the body or health of humans when such a medical device is used by or administered to humans.

ADVERSE EVENT: any event or other occurrence, that reveals any defect in any medical device or that concerns any adverse effect arising from the use thereof.

PRODUCT OWNER *(as set out in the Regulations)*: in relation to a health product, means a person who —

- supplies the health product under his own name, or under any trade mark, design, trade name or other name or mark owned or controlled by him; and
- is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the health product, or for assigning to it a purpose, whether those tasks are performed by him or on his behalf.

2. WHAT ARE REPORTABLE ADVERSE EVENTS?

As a general principle, there should be a pre-disposition to report rather than not to report in case of doubt on the reportability of an AE. Any AE, which meets the three basic reporting criteria listed below, is considered as a reportable AE. The criteria are that:

- an AE has occurred;
- the medical device is associated with the AE;
- the AE led to one of the following outcomes;
  - a serious threat to public health;
  - death of a patient, user or other person;
  - serious deterioration in state of health, user or other person;
  - no death or serious injury occurred but the event might lead to death or serious injury of a patient, user or other person if the event recurs.

An event or other occurrence relating to a medical device represents a serious threat to public health if one or more of the following occur:

- the event or other occurrence is a hazard arising from a systematic failure of the medical device that becomes known to the manufacturer, importer or wholesaler of the medical device;
- the event or other occurrence may lead to the death of, or a serious injury to, a patient, a user of the medical device or any other person;
- the probable rate of occurrence of or degree of severity of harm caused by the hazard was not previously known or anticipated by the product owner of the medical device;
- it becomes necessary for the product owner of the medical device to take prompt action (including the recall of the medical device) to eliminate or reduce the risk of the hazard.

A serious deterioration in state of health can include:

- life-threatening illness or injury;
- permanent impairment of a body function or permanent damage to a body structure;

- a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

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NOTE: Medical devices dealers should encourage feedback from all users, including healthcare professionals, patients and consumers, to establish a comprehensive and effective post-market surveillance system. The analysis and trending of feedback could lead to invaluable insights and improve medical device safety. ◄

NOTE: Adverse events that occur outside of Singapore but where the medical devices have also been supplied in Singapore do not require reporting unless:

- *the registration or licence conditions of those medical devices require so, or*
- *a notice requesting for adverse event information has been issued by the Authority.*

Not all AEs that should be reported involve a death or serious deterioration in health that actually occurred. The non-occurrence of an adverse effect might have been due to other fortunate circumstances or to the timely intervention of health-care personnel. In such cases, it is sufficient that either:

- an AE associated with a medical device happened, and the AE was such that, if it occurred again, it might lead to death or serious deterioration in health; or
- testing, examination of the medical device, information supplied with the medical device, or any scientific literature indicated some factor (e.g. a deterioration in characteristics or performance, or a shortcoming in the information) which could lead to an AE involving death or serious deterioration in health.

For *In Vitro* Diagnostic (IVD) medical devices, it would be sufficient that:-

- an AE associated with an IVD medical device occurred, and
- the AE might lead to death or serious deterioration in health if it happens again;

for the adverse event to become reportable.

In assessing the type of AE, medical practitioner involved or other health-care professional should be consulted wherever practicable.

All persons who register, manufacture, import and supply medical devices should be vigilant for any changes in trends or frequency of occurrences of AEs with regards to medical devices they deal in.

3. ADVERSE EVENTS INVOLVING IN VITRO DIAGNOSTIC DEVICES

Most IVD medical devices do not come into contact with patients and so it is not easy to establish direct harm to patients, unless the IVD medical device itself causes deterioration in the state of health in a patient. However, an adverse event involving an IVD medical device could result in indirect harm as a result of an action taken or not taken on the basis of an incorrect reading obtained with an IVD medical device.

There should always be a predisposition to report even though it may not be easy to establish that a serious deterioration in the state of a patient's health was the result of an erroneous test result obtained with an IVD medical device, or if the harm was the result of an error by the user or third party.

Information supplied by the product owner when inadequate, can lead users, patients or third parties to harm and should be reported. For self-testing IVD medical devices, where a medical decision may be made directly by the user who is the patient, insufficient information on the product presentation could lead to an incorrect use of the IVD medical device or a misdiagnosis. Hence, AEs involving IVD medical devices will most likely result from a consequence of a medical decision or action taken, or not taken, on the basis of result(s) provided by the IVD medical device.

Examples of these types of AEs include (non-exhaustive list):

- misdiagnosis;
- delayed diagnosis;
- delayed treatment;
- inappropriate treatment;
- transfusion of inappropriate materials.

AEs for IVD medical devices may arise due to (non-exhaustive list):

- shortcomings in the design or manufacture of the IVD medical device itself;
- inadequate instructions for use;

- inadequate servicing and maintenance;
- locally initiated modifications or adjustments;
- inappropriate user practice;
- inappropriate management procedures;
- inappropriate environment in which an IVD medical device is used or stored;
- selection of the incorrect IVD medical device for the purpose.

4. ADVERSE EVENT REPORTING TIMELINE

All AEs should be reported immediately and

- not later than 48 hours for events that represents a serious threat to public health;
- not later than 10 days for events that has led to the death, or a serious deterioration in the state of health, of a patient, a user of the medical device or any other person;
- not later than 30 days for events where a recurrence of which might lead to the death, or a serious deterioration in the state of health, of a patient, a user of the medical device or any other person.

The clock for reporting starts as soon as any personnel of the medical device dealers, including sales representatives, is made aware of the AE. If there is uncertainty about whether the AE is reportable, dealers should still submit a report within the timeframe stipulated.

Dealers should not unduly delay the reporting of AE(s) if information is incomplete. The initial report of an AE should contain as much relevant detail as is immediately available, but should not be delayed for the sake of gathering additional information.

Dealers of medical devices are to follow up with a final report within 30 days of the initial reports, detailing the investigation into the AE. If the final report is not available within 30 days, a follow-up report is to be submitted. Follow-up reports may be requested as and when necessary.

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5. ADVERSE EVENT INVESTIGATION

Dealers shall ensure that adequate systems and appropriate procedures in place to investigate, review and report adverse events to HSA, and if necessary, to initiate any field safety corrective action.

HSA may require the following information from the investigation of the adverse event (but not limited to):

- Device analysis results e.g. for device testing carried on returned device or device testing of same lot/batch retained by manufacturer;
- Certificate of Analysis or Certificate of Conformance of affected batch(es);
- Event history log or device log files for devices such as infusion pumps, pacemakers, ventricular assist devices;
- Equipment service reports;
- Review of batch records and any manufacturing deviations associated with the affected batch(es);
- Review of similar complaints, defects, adverse events both locally and globally;
- Analysis of production records;
- Third-party testing or third-party verification of device testing may be required, where necessary;
- Investigation findings and conclusions identifying possible the root cause(s) of the adverse event/incident;
- Description of the remedial, corrective or preventive actions taken or to be taken to prevent similar issue from recurring;
- If no remedial, corrective or preventive actions are taken, justifications as to why it is not necessary shall be provided.

Dealers should provide regular updates to HSA on the progress of the investigation into the root cause. Upon completion of the investigation, a final investigation report with proposed CAPAs, if any, should be submitted to HSA.

Dealers should monitor and assess the effectiveness of the CAPAs and continue to perform trend analyses regularly for any indication of recurring problems requiring attention.

Any decision not to carry out a risk mitigation measure, which would otherwise be required, should be agreed with HSA in advance.

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6. PRESCRIBED FORM AND MANNER FOR SUBMISSIONS

All reports shall be submitted in the following form and manner that the Authority prescribes:-

- Form# MDAR1 for reporting of adverse events not related to clinical trial
- Form# CTB_MD_AE for reporting of adverse events related to clinical trial

NOTE: The CTB_MD_AE form is to be submitted to the Clinical Trials Branch. Refer to the Guidelines on Adverse Event Reporting in Medical Device Clinical Trial to access the report form and more information on reporting requirements.

Submissions may be via email or postal mail as described in the forms. For submissions via email, the use of the interactive pdf AE report form is preferred. If the MS word version of the AE report form is used for submission via email, please ensure a scanned copy of the completed hardcopy AE Report is submitted, together with other accompanying documents/ information. Email size should be under 2MB.

7. WHO SHOULD REPORT?

All persons who register, manufacture, import and supply medical devices in Singapore are required to report AEs involving medical devices, which they have placed on the market. Where a reportable AE involving medical devices placed on the market by more than one person occurs, each person involved should make a report.

8. WHAT HAPPENS WHEN YOU REPORT AN ADVERSE EVENT?

The Authority will acknowledge receipt of the AE report. The Authority will review all AE reports. The information is entered into the computer database for trend analysis.

9. WHAT REGULATORY ACTIONS CAN HSA TAKE?

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HSA may take the following regulatory actions (but not limited to):

- changes to instructions of use, e.g. introduction of specific warnings, reduction in the indications, etc;
- requiring additional safety communications to be distributed, e.g. healthcare professional educational material, patient information leaflet, etc;
- requiring training or retraining/refresher programmes to users;
- requiring additional testing to be carried out. ◄

When a hazard is considered unacceptable, a medical device may be withdrawn from the market.

HEALTH SCIENCES AUTHORITY

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