GHWP

Global Harmonization Working Party

Towards Medical Device Harmonization

FINAL DOCUMENT

Title:	**Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative**
Authoring Group(s):	**Working Group 4: Post-Market**
Date:	September 2024

Dr. Ambrose WONG

Chair, Work Group 4

Table of Content

This guidance document was collaboratively developed by Work Group 4 (WG4) and drafted by Ms. Aisha AL-GHAITHI, Ms. Rui ZHI, Ms. Althea LAU, Ms Chueh-pin CHEN, Dr. Henry HOU and Mr. Wentao Vincent WANG.

1. Preface

This revised guidance on adverse event (AE) reporting for medical devices, including in vitro diagnostic medical devices (IVDs), is developed under the Work Group 4 (WG4) of Global Harmonization Working Party (GHWP), based on the previous guidance document, **Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative (AHWP/WG4/F001:2015)** to promoting the alignment of regulatory standards and establishing a global framework for regulating medical devices across regulatory authorities and industries. This guidance aims to foster the exchange of information and best practices to accelerate the harmonization of medical device regulations and enhance patient safety. Through collaboration and shared knowledge, the GHWP strives to create a coordinated approach that safeguards public health and ensures the timely reporting and evaluation of adverse events related to medical devices.

2. Introduction

2.1 The Global Harmonization Working Party (GHWP) is dedicated to promoting the alignment of regulatory standards to establish a global framework for regulating medical devices (MDs) across regulatory authorities (RAs) and industries (INDs). Its mission includes fostering the exchange of information and best practices among members to accelerate the harmonization of MD regulations.

2.2 The post-market phase of MDs life cycle is a crucial aspect that manufacturers must address by implementing a Medical Device Vigilance System (Vigilance System) to maintain an acceptable benefit-risk balance. The primary goal of the Vigilance System is to enhance the protection of patients, users and others by reducing the likelihood of similar adverse events (AEs) recurring elsewhere. This objective is achieved through the evaluation of reported AEs, the dissemination of information to help prevent such recurrences or mitigate their consequences.

2.3 These guidelines on the Vigilance System are part of a series of GHWP MD Guidelines intended to promote coordinated approach by RAs and INDs in safeguarding public health.

3. Purpose

3.1 The purpose of this guidance is to provide a practical and easy-to-follow reference for RAs and INDs. It aims to support the development and improvement of AE reporting system by summarizing and consolidating international best practices.

3.2 Additionally, this guidance seeks to promote a coordinated approach among RAs and INDs to safeguard public health and ensure the timely and effective management of AE reports in the post-market phase of MDs' lifecycle.

4. Scope

4.1 These guidelines outline the obligations of the Vigilance System concerning manufacturers and their Authorized Representatives (ARs); as well as the role of Regulatory Authority (RA)

4.2 The guidelines detail the necessary steps to be taken when the manufacturer/AR or RA receives information regarding an AE involving an MD.

4.3 This guidance ***excludes*** custom-made MDs, fully refurbished MDs, orphaned MDs, discontinued and obsolete MDs, and MDs that are currently under clinical investigation

5. References

5.1 **Regulation (EU) 2017/745 Medical Device Regulation** (EU MDR)

5.2 **Regulation (EU) 2017/746 In Vitro Diagnostic Medical Device Regulation** (EU IVDR)

5.3 European Commission (2013). ***Guidance document on Market surveillance: Guidelines on a Medical Devices Vigilance System (MEDDEV 2.12/1 rev.8).***

5.4 European Commission (2023). ***Medical Devices MDCG 2023-3 Questions and Answers on vigilance terms and* concepts *as outlined in the Regulation (EU) 2017/745 on medical devices***.

5.5 The GHTF Regulatory Model Authoring Group (2011). ***Ad Hoc GHTF SC Regulatory Model Working Group (GHTF/AHWG-GRM/N1R13:2011).***

5.6 Study Group 1 of Global Harmonization Task Force (2009). ***Definitions of the Terms Manufacturer, Authorized Representative, Distributor and Importer (GHTF/SG1/N055:2009)***.

5.7 Study Group 2 of Global Harmonization Task Force (2006). ***Medical Device Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices (GHTF/SG2/N54R8:2006)***.

5.8 National Competent Authority Report Working Group of International Medical Device Regulator Forum (IMDRF) (2015). ***Medical Devices: Post-Market Surveillance National Competent Authority Report Exchange Criteria and Report Form (IMDRF/NCAR WG/N14 FINAL:2023 (Edition 4))***

5.9 World Health Organization (WHO) (2023). ***WHO Global Model Regulatory Framework for Medical Devices including in vitro diagnostic medical devices***.

5.10 Work Group 4 of the Asian Harmonization Working Party (2015). ***Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative (AHWP/WG4/F001:2015)***

6. Definitions

6.1 **Abnormal use** related to MDs refers to an act or omission of an act by the operator or user of an MD as a result of conduct which is beyond any reasonable means of risk control by the manufacturer (GHTF/SG2/N54R8:2006)

6.2 **Adverse Event (AE)** refers to an event that meeting **ALL** the following **three** basic reporting criteria **(See Section 8.2)** (GHTF/SG2/N54R8:2006):

(i) an event has occurred(1);

(ii) the manufacturer's device is associated with the event;

(iii) the even led to one of the following outcomes:
(a) death of a patient, user or other person; or
(b) serious injury of patient, user or other person; or
(c) 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.

Note:
(1) Examples of an event has occurred, please refer to ***Appendix 1***

6.3 **Authorised Representative (AR)** is defined as any natural or legal person established within a country or jurisdiction who has received a written mandate from the manufacturer to act on his behalf for specified tasks with regard to the latter's obligations under that country or jurisdiction's legislation. (GHTF/SG1/N055:2009)

6.4 **Field Safety Corrective Action (FSCA)** is an action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of an MD. Such actions should be notified via a Field Safety Notice (FSN). The FSCA may include (IMDRF/NCAR WG/N14 FINAL:2023 (Edition 4)

(i) Return of an MD to the manufacturer or its representative;

(ii) Device modification(1);

(iii)Device exchange;

(iv)Device destruction;

(v) Advice given by manufacturer regarding the use of the device (e.g. where the

device is no longer on the market or has been withdrawn but could still possibly be in use, e.g. implants)

Note:
(1) Please refer to IMDRF/NCAR WG/N14 FINAL:2023 (Edition 4) for examples of "(ii) device modification"

6.5 **Field Safety Notice (FSN**) is a communication sent out by a manufacturer or its AR to customer and/or in relation to a FSCA.

6.6 **Intended purposes** refers to the use for which the device is intended according to the data supplied by the manufacturer on the labelling, in the instructions and/or in promotion materials (GHTF/SG2/N54R8:2006)

6.7 **Malfunction or deterioration** means a failure of a device to perform in accordance with its intended purposes when used in accordance with the manufacturer's instructions (GHTF/SG2/N54R8:2006)

6.8 **Manufacturer (or legal manufacturer, also referred to as "product owner" in certain jurisdictions)** is a natural or legal person with responsibilities for the design and/or manufacture of medical device with the intention of making the medical device available for use under his name whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s). (GHTF/SG1/N055:2009 & ISO 13485)

6.9 **Serious**(1) **injury (also referred to as "serious deterioration in the state of health" in some jurisdictions) of a patient, user or any other individual** can include (GHTF/SG2/N54R8:2006):

(i) A life-threatening illness or injury,

(ii) Permanent(2) impairment of a body function or permanent damage to a body structure ,

(iii) A condition necessitating medical or surgical intervention(3) to prevent permanent impairment of a body function or permanent damage to a body structure.

Note:
(1) The interpretation of the term "serious" is not easy, and should be made in consultation with a medical practitioner
(2) The term "permanent" means irreversible impairment or damage to a body structure or damage to a body structure or function, excluding minor impairment or damage
(3) Medical intervention is not is self a serious injury. It is the reason that motivated the medical intervention that should be used to assess the reportability of an event

6.10 **Serious public health threat (also referred to as "significant public health threat" in some jurisdictions)** is any event type which results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action (GHTF/SG2/N54R8:2006).

6.11 **Unanticipated death or unanticipated serious injury** refers to a death or serious injury is considered unanticipated if the condition that leads to an event was not considered in the risk analysis performed during the design and development phase of the device. There must be documented evidence in the design file that such analysis was used to reduce the risk to an acceptable level (GHTF/SG2/N54R8:2006).

6.12 **Use error** in relation to MDs refers to an act or omission of an act, that has a different result than that intended by the manufacturer or expected by the operator of an MD. Use error includes slips, lapses, mistakes and reasonably foreseeable misuse (GHTF/SG2/N54R8:2006).

6.13 **User (or operator)** in relation to MDs includes healthcare institutions, healthcare professionals, lay persons like caregiver or patient, as well as individuals involved in installation or maintenance of the MD.

7. Manufacturers and their Authorized Representatives (ARs)' Role

7.1 The manufacturer/AR must inform the applicable RA in each jurisdiction where the event has occurred or where the MD is marketed according to applicable requirements in each jurisdiction.

7.2 The manufacturer/AR must inform the applicable RA(1) if new information is identified or actions need to be taken following the investigation.

7.3 It is advisable to lean towards reporting rather than not reporting in cases of uncertainty regarding the reportability of an AE. Reporting should be done in accordance with the applicable requirements of the jurisdiction where the event occurred.

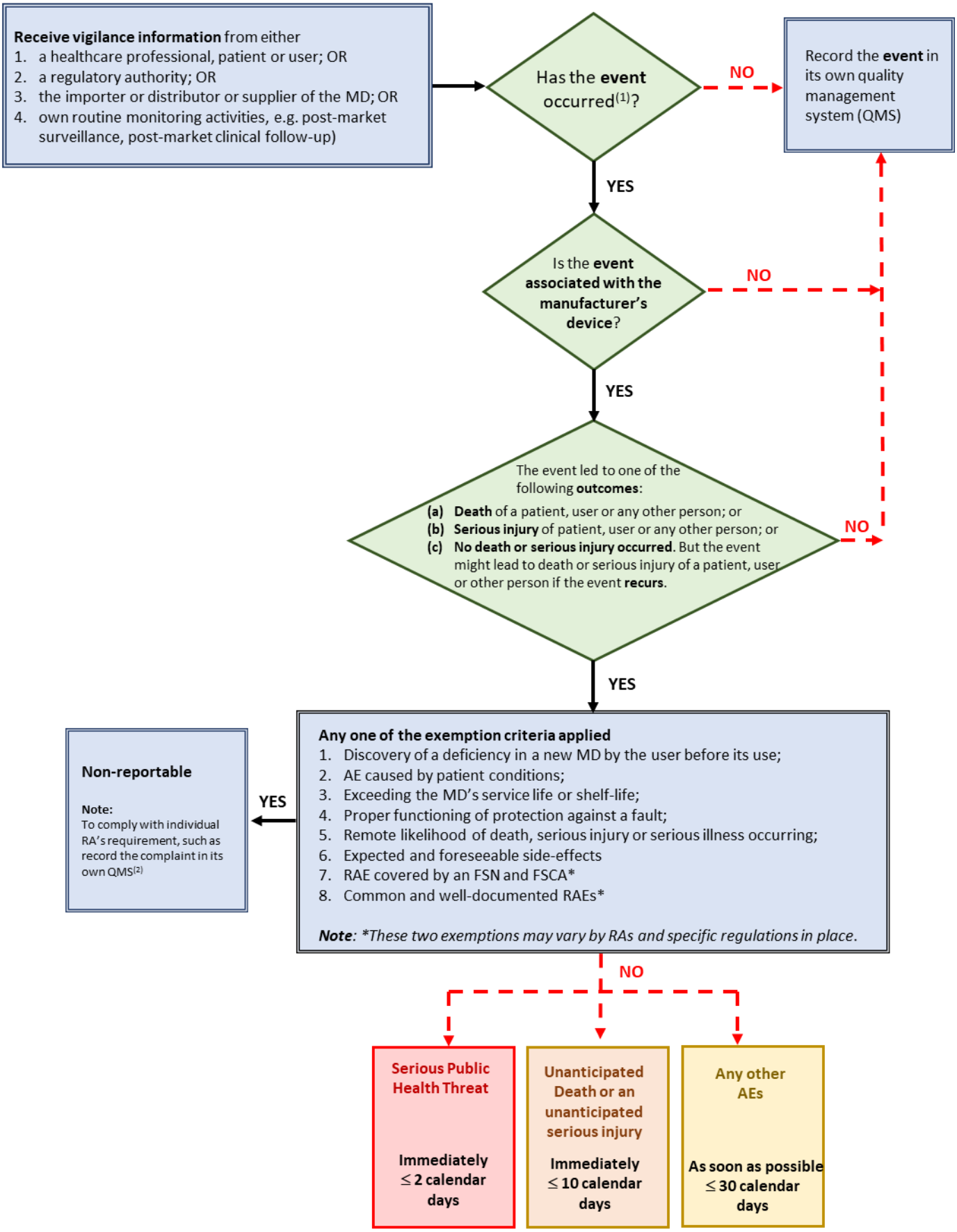
7.4 Any AE reports should not be unnecessarily delayed due to incomplete information. However, manufacturers/ARs should ensure that the initial report meets the requirements specified by the relevant RAs.

7.5 **Flowchart 1** outlines the procedure to be adhered to by MD manufacturers / ARs for handling AEs.

Note:

*(1) **Applicable RA** refers to the relevant RA that has jurisdiction over the marketed medical device or the location where the event occurred.*

Flowchart 1 outlines the procedure to be adhered to by MD manufacturers or ARs for handling AEs



Remarks:
(1) Please refer to **Appendix 1** for details
(2) Individual RA may request the submission of Periodic Summary Report and Trend Report. For details, please see **Section 9** and **Section 10**

8. AE Reporting Requirements for Manufacturer/AR

8.1 This framework promotes a risk-based approach to AE reporting, prioritizing events with the highest potential risk to patient safety. This ensure that significant safety issues are promptly communicated to RAs.

Step 1: Is it an Adverse Event (AE)?

8.2 An event that meeting **ALL** the following **THREE** basic reporting criteria(1) is defined as AE:

(1) An event has occurred *(Please refer to **Appendix 1** for further elaboration);*

(2) the manufacturer's device is associated with the event(2);

(3) the event led to one of the following outcomes:
(a) death of a patient, user or any other person; or
(b) serious injury of patient, user or any other person; or
(c) 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.

Note

(1) **An event that lead to or might lead to a serious public health threat** is considered as an AE and manufacturer/AR is required to report to the relevant RA.

Step 2: Does exemption rules apply? Is the AE Reportable?

8.3 In certain circumstances, the manufacturer/AR of the MD is not obligated to report the AE to RAs, but may adhere to trend reporting(1) instead.

8.4 Once the following exemption criteria are met, the AE would be considered non-reportable. For (i) – (vi), please refer to **Appendix 2** for further information:

(i) Discovery of a deficiency in a new MD by the user before its use;

(ii) AE caused by patient conditions;

(iii) Exceeding the MD's service life or shelf-life;

(iv) Proper functioning of protection against a fault;

(v) Remote likelihood of death, serious injury or serious illness occurring;

(vi) Expected and foreseeable side-effects;

(vii) AEs covered by an FSN and FSCA[(2)];

(viii) Common and well-documented AEs[(2)]

Note:

(1) *Please refer to Section 10 for details.*

(2) *These two exemptions may vary by RAs and specific regulations in place. RA may request the manufacturer / AR to submit periodic summary report instead of individual reporting. For details please refer to Section 9.*

Step 3: When should the AE be reported?

8.5 The reporting timeline considers the severity of the AE. It is advisable that the reporting periods for AE should be calculated in **calendar days**[(1)], including weekdays, public holidays, Saturdays and Sundays.

8.6 General Rule

(i) The reporting period commences on the day following the awareness date of an AE when the manufacturer/AR is **first becomes aware or receives information** about the occurrence of the AE **(i.e. Manufacturer awareness date)**[(2)], not after investigating.

(ii) The reporting timelines for manufacturer/AR are as follows:

(1) AE posing **a serious public health threat** must be reported **immediately**[(3)], and **no later than 2 calendar days (48 hours)** from awareness date of the AE.

(2) AE resulting **in unanticipated death or unanticipated serious injury** must be reported **immediately**[(3)]**,** and **no later than 10 calendar days** from the awareness of the AE.

(3) **All other AE** must be reported **as soon as possible,** and **no later than 30 calendar days** from the awareness of the AE.

Note:

*(1) In some jurisdictions, **working days** is used instead of **calendar days** when calculating reporting periods of AE. Manufacturer/AR should ensure the reporting periods meet the requirements of individual RA to avoid any unnecessary delays.*

*(2) **Manufacturer awareness date** refers to the date when the first employee or representative of the manufacturer's organization receives information, such as a complaint, related to the (potentially) AE. If the handing of these AEs is delegated to an AR or if the manufacturer has outsourced its*

complaint and AE management to a subcontractor, then the reference to manufacturer's organization for the awareness date also includes this designated organization.

(3) ***Immediately*** *refers to without any delay intentionally or negligently caused by the manufacturer/AR*

8.7 Exceptional Circumstances

(i) **New information affecting initial reportability assessment** – If the manufacturer/AR initially determines that an AE does not meet reporting requirements but later obtains new information leading to a change in the reportability assessment, the reporting period starts on the date the manufacturer/AR received the information and determined the AE is reportable.

8.8 **Table 1** summarizes the AE reporting timelines

Table 1 Summary of AE reporting timelines

	Serious public health threat	**Resulting in unanticipated death or unanticipated serious injury**	**All other AEs**
(A) General Rule			
Manufacturer Awareness Date - manufacturer/AR is **first made aware of** or **informed** the AE, before investigation	Day 0	Day 0	Day 0
Initial Report submission	**Immediately** ≤ 2 calendar Days (48 hours)	**Immediately** ≤ 10 calendar Days	**As soon as possible** ≤ 30 calendar Days
(B) Exemptional Circumstances – New information affecting initial reportability assessment			
Manufacturer Awareness Date - Updated information indicates that AE is reportable	Day 0	Day 0	Day 0
Initial Report submission	**Immediately** ≤ 2 calendar Days (48 hours)	**Immediately** ≤ 10 calendar Days	**As soon as possible** ≤ 30 calendar Days

Step 4: How to report the AE?

8.9 To ensure timely reporting, the manufacturer/AR may submit an initial AE report followed by a subsequent follow-up AE report only (1) when new, significant information becomes available that affects the original assessment; or (2) if additional actions are required; or (3) upon RA's request. A delay in submitting the initial report, for reasons such as incomplete information provided by the healthcare facility, end user or other relevant parties, is not considered justified. However, the initial report should include all available information, with the understanding that additional details can be provided through follow-up reports as necessary.

8.10 The different types of AE reports are as follows:

(i) **Initial report –** this is the first information submitted by the manufacturer/AR regarding an AE;

(ii) **Follow-up report –** This report provides supplementary information about the event that was not available at the time of the initial report.

(iii) **Final report –** This is the last report that the manufacturer/AR intends to submit regarding the AE(1). The final report may also be the first report(2).

8.11 **Appendix 3** provides detailed information regarding the AE reports

Note:

(1) Final report usually concludes the investigation of the AE, including the follow-up, corrective and/or preventive actions taken by the manufacturers if required.

(2) In some circumstances, initial report and final report are combined into one single submission.

9. Periodic Summary Reporting by Manufacturer/AR (Upon RA's request)

9.1 **Under specific circumstances, and at the discretion of the RA,** the manufacturer/AR may be requested to submit a periodic summary report by the RA instead of individual reporting for:

(i) **AEs covered by an FSN and FSCA** – AEs already addressed in an FSN and followed by an FSCA do not require individual reporting. Instead, they can be included in Periodic Summary Reports as agreed with the relevant RA.

(ii) **Common and well-documented AEs** – AEs identified in the MD's risk analysis with corresponding AE reports reviewed by the manufacturer and relevant RAs. They should be clinically known in terms of root cause and qualitative or

quantitative predictability. These AEs may be exempt from individual reporting by RA and can be transitioned to Periodic Summary Reporting.

9.2 **Appendix 4** provides suggested information for a periodic summary report.

10. Trend Reporting by Manufacturer/AR (Upon RA's request)

10.1 Trend reporting is initiated when there is a statistically significant increase in the AEs that are generally not considered reportable. Specific trigger levels are established to determine when this threshold for reporting is met. **At the discretion of the RA,** the manufacturer/AR may be required to provide trend reports once the RA reviews one or more initial reports. This is particularly relevant when there is a noticeable increase in:

(i) **AEs that have already report:** This includes AEs covered by an FSN and FSCA, as well as those that are common and have been well-documented; or

(ii) **AEs that are exempted from reporting**: These are AEs that fall under the exemptions detailed in Section 8.3 (i) – (vi); or

(iii) **AEs that are usually not subject to reporting**, such as those occurring outside the regulatory jurisdiction indicating potentially important changes in product safety.

10.2 The criteria for trend reporting should be mutually agreed upon by the manufacturer/AR and individual RA, and the reports should be submitted in an agreed format and frequency for specific types of MDs and AEs.

10.3 **Appendix 5** provides suggested information for a trend report.

11. AE Reporting of Use Error and Abnormal Use by Manufacturer/AR

11.1 Any use error that leads to the death or serious deterioration in an individual's state of health or poses serious public health treat, must be reported by the manufacturer / AR to the RA within specific timeline.

11.2 Manufacturer/AR are not required to report abnormal use to RAs, as abnormal use situations should be managed by healthcare facilities and relevant RAs under specific scheme that are not addressed in this guidance document.

12. Regulatory Authority's (RA) Role

12.1 The RA should promptly send an acknowledgement of receipt to the sender upon receiving the AE report.

12.2 The RA should assess the report in collaboration with the manufacturer/AR, where practicable, provide advice as necessary, and intervene when required.

12.3 AE reports received from users should be promptly forwarded by the RA to the manufacturer/AR without delay or alternation. Patient confidentiality must be upheld during the process.

12.4 The RA should review the risk assessment conducted by the manufacturer/AR of the reported AE, ensuring it aligns with a risk-based approach. The RA may intervene as necessary to ensure the assessment is adequate and that the most significant risks are addressed appropriately.

12.5 The RA should monitor the investigation and subsequent actions of the manufacturer/AR and may intervene at any point as needed. Aspect of monitoring may include the direction, conduct, progress and outcome of the investigation.

12.6 The RA may take any further action it deems appropriate, such as consulting and inspecting with manufacturer/RA, where possible.

Appendix 1 – Elaboration of AE Reporting Criteria

AE Reporting Criteria	Elaboration
(i) **An event has occurred**	**(1) Examples of an event has occurred:** a. Malfunction of an MD when used in accordance to the information provided, e.g. a sudden software error causing incorrect assessments and treatment delivery to a patient b. Deterioration in the characteristics or performance of an MD[1], e.g. failures in sterilisation process due to manufacturing errors; or UV degradation, like cracking or disintegration from exposure to ultraviolet radiation c. Use error due to ergonomic features[1], e.g. low touchscreen sensitivity on a patient monitor, can cause incorrect function activation. This may lead to user mistakenly pressing an adjacent button, initiating an unintended function and causing treatment delays. d. Inadequacy in the information provided by the manufacturer, e.g. users discovers that insufficient details are provided on cleaning methods for reusable surgical instruments e. Unclear instructions in the labelling or the manufacturer's IFU, where information is not presented in a manner easily understood by the intended user. f. Undesirable side-effects[2] such as allergic skin reactions like nickel allergies or complications in wound

AE Reporting Criteria	Elaboration
	therapies.
(ii) The manufacturer's device is associated with the event	**(1) Establish causal relationship** When evaluating the connection between their MDs and an event, the manufacturer should consider factors like (i) Medical plausibility; (ii) Healthcare professional's opinions, (iii) Their own initial assessment findings (iv) Documented information (v) Evidence of similar AEs; and (vi) Any other relevant data the manufacturer posses Establishing this link can be challenging, especially in cases involving multiple MDs and medications. In complex scenarios, it is important to presume that an MD might have played a role in the AE. Therefore, the manufacturer should approach their assessment with caution and refrain from drawing definitive conclusions. If there is uncertainty, the manufacturer/AR must still submit the AE report to RAs.
(iii) The event led to one of the following outcomes: **(a) death of a patient, user or any other person; or** **(b) serious injury of patient, user or any other person; or** **(c) 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** (d) **Serious public health threat**	**(1) AE indirectly lead to a serious injury** In certain instances, an MD may not directly or immediately cause physical injury or damage to a person's health due to its intended use, but rather results in indirect harm. **Indirect harm** can arise because of medical decisions, actions taken or not taken based on information or results provided by an MD, or as a consequence of a specific treatment.

AE Reporting Criteria	Elaboration
	Examples of indirect harm may include: (1) Misdiagnosis (2) Delayed diagnosis (3) Delayed treatment (4) Inappropriate treatment (5) Lack of treatment (6) Transfusion of inappropriate materials **(2) Examples of serious public health treats** a. Communicable diseases, such as human immunodeficiency virus (HIV), Creutzfeldt-Jakob Disease (CJD), Ebola, Zika virus, severe acute respiratory syndrome (SARS), Coronavirus disease (COVID-19), b. Events involving a high risk of exposure to a disease (e.g. cancer) following the use of an MD, impacting a significant portion of the population, a specific patient group (e.g. diabetics, cardiac patients, etc.) or a vulnerable population (e.g. children, pregnant women, etc.) c. Exposure to toxic compounds with potential harmful effects on humans d. Proliferation of falsified or incorrectly labelled MDs leading to numerous AEs, for example, the distribution of non-sterile MDs falsely labelled as sterile e. Cyberattack targeting life-saving or life-supporting MDs

AE Reporting Criteria	Elaboration

Notes

[1] ***Use-error due to ergonomic features*** *refers to errors caused by MD design features intended to facilitate safe and effective use by the user.* ***Ergonomic features*** *include physical aspects designed to ensure safe and efficient user-device interaction such as measurement features, displays, alarms, and software menus.*

[2] ***Undesirable side-effects*** *are unintended and unwanted medical manifestation in the human body, resulting from the normal use of MDs. These effects are not due to malfunction, deterioration or inadequate manufacturer information. Treatment failures are NOT considered undesirable side-effects.*

Appendix 2 – Criteria for Non-reportable AE

Exemption Rules	Examples
(i) Discovery of a deficiency in a new MD by the user before its use *Deficiencies in MDs that would typically identified by the user, even without specific instructions in the manufacturer's provided instructions for use (IFU), and do not result in serious injury, are not required to be reported.*	(1) A malfunction was detected during an inflation test performed by the user before inserting the balloon catheter into the patient, as per the accompanying IFU. Another balloon was used, and no injury to the patient occurred. (2) The packaging of a sterile single-use MD is labelled with the caution "**do not use if the packaging is opened or damaged**". Visible damage to the packaging was noted before use, and an MD was not used. (3) The tip protector of an intravenous administration set fell off during distribution, creating a non-sterile fluid pathway. The intravenous administration set was not used. (4) A vaginal speculum showed multiple fractures and fell apart when the handle was activated. An MD was not used. (5) The user discovered that a bottle labelled "lyophilized" in an IVD testing kit contains fluid before use.
(ii) AE caused by patient conditions *If the manufacturer/AR determines that the root cause of the event is related to the patient condition, reporting of the AE is not required. These conditions may either be pre-existing or develop during MD use.* *To substantiate the decision not to report, the manufacturer/AR must possess information affirming that an MD operated as designed and did not lead to or exacerbate*	(1) An orthopedic implant requires early revision due to loosening caused by the patient developing osteolysis, which is not deemed a direct consequence of the implant failure. This assessment would require conformation from a medical expert. (2) A patient with end-stage renal disease passed away following dialysis treatment. The manufacturer's investigations confirmed an MD was operating as

Exemption Rules	Examples
death or serious deterioration in state of health. A medical qualified individual would concur with this condition. It is advisable for the manufacturer/AR to engage a clinician in decision-making process	intended, and the AE was not linked to an MD.
(iii) Exceeding the MD's service life or shelf-life *If the sole reason for an event is that an MD surpassed its service life or shelf-life as outlined by the manufacturer, and the failure mode is not uncommon, the AE does not necessitate reporting.* *The service life or shelf-life must be clearly defined by the manufacturer and documented in the master record (technical file) and, when applicable, in the IFU or labelling.* *Service life or shelf-life may encompass duration or usage for which an MD is designed to remain operational after being manufactured, put into service, and maintained as specified. The assessment for reporting should be guided by the information in the master record or the IFU.*	(1) Loss of sensing occurred after a pacemaker had reached the end of life. The elective replacement indicator activated as per an MD specification within the designated timeframe. Surgical intervention for pacemaker replacement is necessary. (2) Inadequate contact of the defibrillator pads with the patient was noted. Defibrillation could not be performed effectively due to insufficient chest contact. Although the self-life of the pads was indicated, it was exceeded. (3) A patient was hospitalized with hypoglycemia due to an incorrect insulin dosage prompted by a blood glucose test result. Investigation revealed that the test strip was used pass the expiry date specified by the manufacturer (4) A drill bit was used beyond its designated service life. It fractured during an invasive procedure, leading to extended operation time due to challenges in retrieving the broken parts.
(iv) Proper functioning of protection against a fault *AEs which did not lead to serious deterioration in state of health or death, because a design feature protected against a fault becoming a hazard do not need to be reported. If an alarm system is used, the*	(1) An infusion pump experiences a malfunction and stops, but issues an appropriate alarm (in accordance with relevant standards), and no harm comes to the patient. (2) Microprocessor-controlled radiant warmers malfunction and sound an appropriate

Exemption Rules	Examples
concept of this system should be generally acknowledged for that type of product	audible alarm (in compliance with relevant standards), with no negative impact on patient's health. (3) During radiation treatment, the automatic exposure control activates, leading to treatment cessation. Despite the patient receiving a suboptimal dose, there is no excessive radiation exposure. (4) A laboratory analyser halts analysis due to a malfunction in the sample pipetting module, but provides the user with the necessary error message. User intervention or immediate remote assistance from the manufacturer allows the analyzer to resume analysis, yielding accurate results.
(v) Remote likelihood of death, serious injury or serious illness occurring *AEs where the reporting if no actual death or serious deterioration in state of health occurred, and the risk has been thoroughly assessed and documented as acceptable in a comprehensive risk evaluation.* *However, if an AE resulting in death or serious deterioration in state of health occurs, it must be reported, and a re-evaluation of the risk is essential. If the reassessment confirms that the risk remains insignificantly low, previous AEs of the same nature do not need to be reported retroactively.* *Nevertheless, decisions to omit reporting subsequent failures of a similar nature must be recorded. Any changes in the trend of these less severe outcomes, typically an increase, should be reported.*	(1) The pacemaker malfunction occurred only when a specific setting was use. However, since the patient is currently using a different setting, there is no risk of health injury.

Exemption Rules	Examples
(vi) Expected and foreseeable side-effects *Expected and foreseeable side effects that meet the following criteria:* *a. clearly identified in the manufacturer's labelling; and* *b. clinically well-known* as foreseeable with certain qualitative** and quantitative predictability when an MD is used and performed as intended; and* *c. documented in an MD master record with appropriate risk assessment before any AE occur; and* *d. clinically acceptable in terms of the individual patient benefit* *are typically not required to be reported.* *It is advisable for the manufacturer to involve a clinician in this decision-making process. If the manufacturer observes a change in the risk-benefit ratio, such as an increase in frequency or severity of reported expected side effects that have led or may lead to death or serious deterioration of state of health, this change must be considered a performance characteristic deterioration of an MD. A trend report should be sent to RA.* **Notes:** **Certain events are widely recognized in the medical, scientific, or technology field, while others may have been identified during clinical investigation or clinical practice, and labelled by the manufacturer.* ***The factors that contribute to these side effects can be outlined, although numerical prediction may sometimes pose challenges*	(1) A patient sustains a second-degree burn while using an external defibrillator in an emergency. The risk assessment acknowledges that such burns may occur for potential patient benefit and is cautioned in the IFU. The frequency of burns falls within the range specified in an MD master record. (2) A patient with a mechanical heart valve developed endocarditis ten years after implantation, resulting in death. The risk assessment indicates that endocarditis at this stage is clinically acceptable for the patient benefit, and the IFU warns of this potential side effect. (3) Placement of a central line catheter causes anxiety and shortness of breath in a patient, both of which are recognized and labelled as side effects

Appendix 3 - Adverse Event (AE) Report Format (Manufacturer/AR to the RA)

ADVERSE EVENT

Manufacturer/AR's Report

(GHWP/WG4/F003 ver. 1.0)

I. Administrative Information		
1. Recipient (Regulatory Authority (RA))	(Name)	
	(Address)	
2. Date of this report (YYYY/MM/DD)		
3. Reference Number	Assigned by Manufacturer / AR	
	Assigned by RA	
4. Type of AE Report		☐ Initial Report ☐ Follow-up Report (Follow-up Number ____) ☐ Combined Initial and Final Report ☐ Final Report
5. Does the AE represent a significant public health threat? *(Please response to Q6 regardless of whether your answer is affirmative or negative)*		☐ Yes ☐ No
6. Classification of AE		☐ Death ☐ Unanticipated serious deterioration in state of health ☐ All other reportable AEs

7. Other RAs to which this report was also sent		

II. Information of the Reporter

1. Reporter	Role	☐ Manufacturer ☐ Authorized Representative (AR) ☐ Others, please specify _____
	Name	
	Contact Person	
	Address	
	Phone	
	Fax	
	E-mail	

III. Medical Device Information

1. **Class of the medical device**	☐ General Medical Device (GMD)	☐ Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4

		☐ In Vitro Diagnostic Medical Device (IVDMD)	☐ Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4
2. Nomenclature	System	☐ GMDN ☐ Others, please specify _____	
	Code		
	Description		
3. **Commercial name / brand name / make**			
4. Model Number			
5. Catalogue Number			
6. **Serial number(s)** *(if applicable)*			
7. Lot/batch number(s) *(if applicable)*			
8. Software version number *(if applicable)*			
9. Device manufacturing date (YYYY/MM/DD)			
10.Expiry Date (YYYY/MM/DD)			
11.Implant Date (for implants only) (YYYY/MM/DD)			
12. Explant Date (for implants only) (YYYY/MM/DD)			

13. Duration of implantation *(to be filled is the exact implant or explant dates are unknown)*		
14. Accessories / associated device *(if applicable)*		
15. Conformity Assessment Body *(if applicable)*		
16. Manufacturer	Name	
	Contact Person	
	Address	
	Phone	
	Fax	
	E-mail	
17. AR	Name	
	Contact Person	
	Address	
	Phone	

	Fax	
	E-mail	

IV. Information of the Adverse Event (AE)

1. **User Reference Number** *(if applicable)*	
2. Manufacturer/AR awareness date (YYYY/MM/DD)	
3. Date the AE occurred (YYYY/MM/DD)	
4. Description of the AE	
5. Adverse Event Terminology *(Optional)*[1]	
6. Number of affected people involved *(if known)*	
7. Number of medical devices involved *(if known)*	
8. Medical Device current location / disposition *(if known)*	
9. Operator of the medical device at the time of AE *(select one)*	☐ Patient ☐ Health care professional ☐ Others, please specify_____
10. Usage of the medical device *(select one)*	☐ Initial use ☐ Reuse of a reusable medical device ☐ Reuse of a single use medical device

		☐ Re-serviced / refurbished medical device ☐ Problem noted prior use ☐ Others, please specify _____
11. Patient information	Outcome	
	Age of the patient at the time of AE, if applicable	
	Gender, if applicable	☐ Male ☐ Female ☐ Others, please specify _____
	Weight in kilograms, if applicable	
	Remedial action taken by the healthcare facility relevant to the care of the patient	
12. Health care facility information	Name	
	Contact person	
	Address	
	Phone	
	Fax	
	E-mail	

V. Manufacturer's Preliminary Comments (For Initial Report / Follow-up Report)	
1. Manufacturer's preliminary analysis	
2. Initial corrective actions/preventive actions implemented by the manufacturer	
3. Expected date of next report (YYYY/MM/DD)	
VI. Results of Manufacturers Final Investigation (Final Report)	
1. **Manufacturer's device analysis results**	
2. Identified actions	☐ No action ☐ Remedial actions ☐ Corrective actions ☐ Preventive actions ☐ FSCA (please see the attachment) ☐ Others, please specify _____

	Description of the identified actions
3. Time schedule for the implementation of the identified actions	
4. Final comments from the manufacturer	☐ No action required ☐ Additional surveillance of medical device in use ☐ Preventive action on future production ☐ FSCA (please see the attachment) ☐ Others, please specify _____
	Elaboration of the Final comments
5. Further investigations	☐ Yes ☐ No
	Description of further investigations
6. Is the manufacturer/AR aware of similar AE with this type of medical device with a similar root cause?	☐ Yes ☐ No
	If yes: Number of similar incidents: _____

	Which countries and the report reference numbers of the incidents

VII. Comments from RA (For RA Official Use Only)

1. Comments	☐ No action required ☐ Follow-up report ☐ Final report ☐ FSCA ☐ Others, please specify _____
	Elaboration of comments

VIII. Disclaimer

I affirm that the submitting of this report, it is not an admission of liability for the manufacturer, AR, user, patient or RA regarding the AE and its consequences. Furthermore, it does not imply that the content of this report, in itself, represent a conclusion by the manufacture /AR or the RA, and is deemed complete or accurate, nor does it suggest that the listed medical device(s) failed or caused or contributed to the alleged death or deterioration in the state of the health of any person.

I confirm that the information provided above is accurate to the best of my knowledge.

_____

Name:

Date (YYYY/MM/DD):

Note: [1] RA has the discretion to choose whether or not to include the Adverse Event Terminology (such as IMDRF AET) in adverse event reporting. For IMDRF AET, please refer to IMDRF/GHTF N43R1: IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes https://www.imdrf.org/sites/defau lt/files/2021-09/imdrf-cons- imdrf-terminologies-caer.pdf

Appendix 4 - Adverse Event (AE) Periodic Summary Report Format (Manufacturer/AR to the RA)

ADVERSE EVENT

Manufacturer/AR's Periodic Summary Report (PSR)

(GHWP/WG4/F003 ver. 1.0)

I. Administrative Information		
1. Recipient (Regulatory Authority (RA))	(Name)	
	(Address)	
2. Date of this report (YYYY/MM/DD)		
3. Reference Number	Assigned by Manufacturer / AR	
	Assigned by RA	
4. Type of Periodic Summary Report (PSR)		☐ Initial report ☐ Follow-up report (Follow-up Number ____) ☐ Final report
II. Information of the Reporter		
1. Reporter	Role	☐ Manufacturer ☐ Authorized Representative (AR) ☐ Others, please specify _____
	Name	
	Contact Person	

	Address	
	Phone	
	Fax	
	E-mail	

III. Medical Device Information

1. **Class of the medical device**		☐ General Medical Device (GMD)	☐ Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4
		☐ In Vitro Diagnostic Medical Device (IVDMD)	☐ Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4
2. Nomenclature	System	☐ GMDN ☐ Others, please specify _____	
	Code		
	Description		
3. **Commercial name / brand name / make**			

4. Model Number		
5. Catalogue Number		
6. **Serial number(s)** *(if applicable)*		
7. Lot/batch number(s) *(if applicable)*		
8. Software version number *(if applicable)*		
9. Accessories / associated device *(if applicable)*		
10. **Conformity Assessment Body** *(if applicable)*		
11. Manufacturer	Name	
	Contact Person	
	Address	
	Phone	
	Fax	
	E-mail	
12. AR	Name	
	Contact Person	

	Address	
	Phone	
	Fax	
	E-mail	

IV. Information on Periodic Summary Report (PSR)

1. Types of PSR	☐ AEs covered by an FSN and FSCA **FSN/FSCA Ref. no**.:
	☐ Common and well-documented AE **Document Ref no.:**
	☐ Others, please specify _____
2. Stage of PSR based on	☐ Observed Failure mode ☐ Root cause
3. Description of AE for PSR	
4. Adverse Event Terminology *(Optional)*[1]	
5. Summary period agreed	☐ Monthly (Every month) ☐ Bi-monthly (Every 2 months) ☐ Quarterly (Every 3 months) ☐ Bi-Annually (Every 6 months) ☐ Annually (Every 12 months) ☐ Others, please specify _____

6. Summary of the data collected during the period				
Date of Periodic Summary Report (YYYY/MM/DD)	**New AEs this period**	**Total number AEs via PSR**	**Total number of AEs resolved**	**Total number of unresolved AEs (in progress)**

v. Manufacturer's comments / investigation results

1. **Investigation update(s) for this period**	
2. Corrective actions/preventive actions implemented by the manufacturer	
3. Identified actions for this period	☐ Yes ☐ No

4. Details of identified actions	☐ No action required ☐ Corrective Actions ☐ Preventive actions ☐ FSCA (please see the attachment) ☐ Others, please specify _____
	Description of identified actions
5. Expected date of next Periodic Summary Report (YYYY/MM/DD)	

VI. Comments from RA (For RA Official Use Only)

1. Comments	☐ No action required ☐ Follow-up report ☐ Final report ☐ FSCA ☐ Others, please specify _____
	Elaboration of comments

VII. Disclaimer

I affirm that the submitting of this report, it is not an admission of liability for the manufacturer, AR, user, patient or RA regarding the AE and its consequences. Furthermore, it does not imply that the content of this report, in itself, represent a conclusion by the manufacture /AR or the RA, and is deemed complete or accurate, nor does it suggest that the listed medical device(s) failed or caused or contributed to the alleged death or deterioration in the state of the health of any person.

I confirm that the information provided above is accurate to the best of my knowledge.

_____

Name:

Date (YYYY/MM/DD):

Note: [1] RA has the discretion to choose whether or not to include the Adverse Event Terminology (such as IMDRF AET) in adverse event reporting. For IMDRF AET, please refer to IMDRF/GHTF N43R1: IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes https://www.imdrf.org/sites/defau lt/files/2021-09/imdrf-cons- imdrf-terminologies-caer.pdf

Appendix 5 - Adverse Event (AE) Trend Report Format (Manufacturer/AR to the RA)

ADVERSE EVENT

Manufacturer/AR's Trend Report

(GHWP/WG4/F003 ver. 1.0)

I. Administrative Information		
1. Recipient (Regulatory Authority (RA))	(Name)	
	(Address)	
2. Date of this report (YYYY/MM/DD)		
3. Reference Number	Assigned by Manufacturer / AR	
	Assigned by RA	
4. Type of AE Trend Report		☐ Trend Initial ☐ Trend Follow-up (Follow-up Number ____) ☐ Trend Final
5. **Does the AE / Trend represent a significant public health threat?**		☐ Yes ☐ No
6. Other RAs to which this report was also sent		
II. Information of the Reporter		
1. Reporter	Role	☐ Manufacturer ☐ Authorized Representative (AR) ☐ Others, please specify _____

	Name		
	Contact Person		
	Address		
	Phone		
	Fax		
	E-mail		
III. Medical Device Information			
1. **Class of the medical device**		☐ General Medical Device (GMD)	☐ Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4
		☐ In Vitro Diagnostic Medical Device (IVDMD)	☐ Class 1 ☐ Class 2 ☐ Class 3 ☐ Class 4
2. Nomenclature	System	☐ GMDN ☐ Others, please specify_____	
	Code		
	Description		

3. **Commercial name / brand name / make**		
4. Model Number		
5. Catalogue Number		
6. Serial number(s) *(if applicable)*		
7. Lot/batch number(s) *(if applicable)*		
8. Software version number *(if applicable)*		
9. Accessories / associated device *(if applicable)*		
10. **Conformity Assessment Body** *(if applicable)*		
11. Manufacturer	Name	
	Contact Person	
	Address	
	Phone	
	Fax	
	E-mail	

12. AR	Name	
	Contact Person	
	Address	
	Phone	
	Fax	
	E-mail	

IV. Information on Trend Report	
1. Date of the trend was identified (YYYY/MM/DD)	
2. Description of the identified trend	
3. Time period of trend analysis	
4. Adverse Event Terminology *(Optional)*[1]	
5. Established trigger level	
6. Have any of the trended events been submitted individually as AE under vigilance system?	☐ Yes ☐ No
	If yes, please list how many and to which RAs

V. Manufacturer's Preliminary Comments (For Initial Report / Follow-up Report)	
1. Manufacturer's preliminary analysis into causes of trend	
2. Initial corrective actions/preventive actions implemented by the manufacturer	
3. Expected date of next report (YYYY/MM/DD)	
VI. Results of Manufacturers Final Investigation into trend (Final Report)	
6. **Manufacturer's trend analysis results**	
7. Identified actions	☐ No action ☐ Remedial actions ☐ Corrective actions ☐ Preventive actions ☐ FSCA (please see the attachment) ☐ Others, please specify _____
	Description of the identified actions
8. Time schedule for the implementation of the identified actions	

9. Final comments from the manufacturer	
10. Further investigations	☐ Yes ☐ No
	Description of further investigations

VII. Comments from RA (For RA Official Use Only)

2. Comments	☐ No action required ☐ Follow-up report ☐ Final report ☐ FSCA ☐ Others, please specify _____
	Elaboration of comments

VIII. Disclaimer

I affirm that the submitting of this report, it is not an admission of liability for the manufacturer, AR, user, patient or RA regarding the AE and its consequences. Furthermore, it does not imply that the content of this report, in itself, represent a conclusion by the manufacture /AR or the RA, and is deemed complete or accurate, nor does it suggest that the listed medical device(s) failed or caused or contributed to the alleged death or deterioration in the state of the health of any person.

I confirm that the information provided above is accurate to the best of my knowledge.

_____

Name:

Date (YYYY/MM/DD):

Note: [1] RA has the discretion to choose whether or not to include the Adverse Event Terminology (such as IMDRF AET) in adverse event reporting. For IMDRF AET, please refer to IMDRF/GHTF N43R1: IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes https://www.imdrf.org/sites/defau lt/files/2021-09/imdrf-cons- imdrf-terminologies-caer.pdf