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Global Harmonization Working Party

Towards Medical Device Harmonization

PROPOSED DOCUMENT

Title: **Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative**

Authoring Group(s): **Working Group 4: Post-Market**

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1. Preface

This revised guidance on adverse event reporting for medical devices is developed under the Working Group 4 of Global Harmonization Working Party (GHWP) 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 among members 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 serious 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 standardized framework for the reporting of AEs related to MDs, as part of the Vigilance System. By outlining the obligations of manufacturers, Authorized Representatives (ARs), and RAs, this guidance aims to enhance patient safety, reduce the likelihood of AEs recurring, and facilitate the dissemination of information to prevent or mitigate potential risks associated with MDs.

3.2 Additionally, this guidance seeks to promote a coordinated approach among 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:

(i) Manufacturers and their Authorized Representatives (ARs)

(ii) 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. Information on AEs that must be reported under the Vigilance System may be brought to the manufacturer/AR's attention through post-market surveillance to assess the knowledge gained from MDs during the post-production phase or through other applicable channels.

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

5. References

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

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

5.3 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*.

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

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

5.6 Study Group 2 of Global Harmonization Task Force (2006). *Medical Device Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices (GHTF/SG2N54R8:2006).*

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

5.8 IEC 60601-1-6:2010 Medical electrical equipment – Part 1-6: General requirements for basic safety and essential performance – Collateral standard: Usability

5.9 Working 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 means of risk control by the manufacturer. *(IEC 60601-1-6)*

6.2 **Adverse Event (AE)** refers to any *malfunction or deterioration in the characteristics or performance of an MD* that has been released onto the market. *(modified from EU MDR)*

6.3 **Authorised Representative (AR)** is defined as any individual or entity *(such as a corporation, a partnership or an association)* located within a specific country or jurisdiction who has been granted written authority by the manufacturer to carry out designated tasks on behalf of the manufacturer in relation to the latter's obligations under the legislation of that country or jurisdiction. *(modified from 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 that is already placed on the market. Such actions, whether associated with direct or indirect harm, should be reported and communicated to customer and/or user via a Field Safety Notice (FSN). The FSCA may include

(i) Return of an MD to the supplier;

(ii) Device modification*;

(iii)Device exchange;

(iv)Device destruction;

(v) Retrofit by purchaser of manufacturer's modification or design change;

(vi)Advice given by manufacturer regarding the use of the device and/or the follow up of patients, users or others*

Note:
**Please refer to IMDRF/NCAR WG/N14 FINAL:2023 (Edition 4) for examples of "(ii) device modification" and "(vi) advice given by manufacturer regarding the use of the device and/or the follow up of patients, users or others"*

(modified from IMDRF/NCAR WG/N14 FINAL:2023 (Edition 4))

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. *(MEDDEV 2.12/1 rev.8)*

6.6 **Intended purposes** refers to the specific use for which an MD is intended based on the information provided by the manufacturer on the labelling and in the instructions *(modified from GHTF/SG2N54R8:2006)*

6.7 **Manufacturer (or legal manufacturer, also referred to as "product owner" in certain jurisdictions)** is any individual or entity *(such as a corporation, a partnership or an association)* responsible for design or production of an MD with the purpose of making an MD available for use under their name, regardless of whether an MD is designed or produced by that individual/entity or by another party on their behalf. *(modified from GHTF/SG1/N055:2009)*

6.8 **Reportable Adverse Event (RAE)** pertains to any AE that has *directly or indirectly resulted in*, OR has *potential resulted* in:

(i) The death of a patient, user or any other individual; or

(ii) The temporary or permanent serious deterioration in the state of health of patient, user or any other individual; or

(iii) A significant public health threat

6.9 **Serious deterioration in the state of health (also referred to as "serious injury") of a patient, user or any other individual** encompasses:

(i) A life-threatening illness or injury,

(ii) Permanent or temporary impairment of a body structure or a body function (including impairments resulting in diagnosed psychological trauma),

(iii) A condition requiring hospitalization or extension of current hospitalization,

(iv) Medical or surgical intervention to prevent (i) or (ii), such as:
   a. Professional medical care or unexpected additional medical treatment,
   b. Clinically significant prolongation of a surgical procedure,

(v) Fetal distress, fetal death, any congenital abnormality (including congenital physical or mental impairment), or birth defects.

193

194 *(modified from GHTF/SG2N54R8:2006)*

195

196 *6.10* **Significant public health threat** is an event that poses an immediate risk of death,
197 serious deterioration in the state of an individual's health, or serious illness, that
198 necessitates urgent intervention.

199

200 ***Note:*** *Such events can lead to significant illness or death in humans and are*
201 *uncommon or unforeseen for the specific location and time. These occurrences may*
202 *involve multiple deaths happening rapidly or events that are notably unusual and*
203 *alarming as a potential public health hazard, such as human immunodeficiency*
204 *virus (HIV), Creutzfeldt-Jacod Disease (CJD), Ebola or Coronavirus disease (COVID-*
205 *19).*

206

207 *(modified from GHTF/SG2N54R8:2006)*

208

209 6.11 **Unanticipated** is a condition that leads to an event not previously considered
210 during the risk analysis conducted in the device's design and development phase.
211 Such RAE may be unanticipated due to reasons like:

212

213 (i) Limited historical information (rare cases);

214

215 (ii) Changes in the context or situation;

216

217 (iii) Altered patient, healthcare professional or user outcomes;

218

219 (iv) Off-label use of the device.

220

221 *(modified from IMDRF/NCAR WG/N14 FINAL:2023 (Edition 4))*

222

223 6.12 **Use error** in relation to MDs refers to an act or omission of an act, that has a
224 different result to that intended by the manufacturer or expected by the operator
225 of an MD. *(IEC 60601-1-6)*

226

227 6.13 **User (or operator)** in relation to MDs includes healthcare institutions, healthcare
228 professionals, lay persons like caregiver or patient, as well as individuals involved in
229 installation or maintenance of the MD.

230

231

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

233

234 7.1 The manufacturer/AR must inform the RAs about any reportable adverse event (RAE)
235 and provide an initial report for recording and evaluation. An initial report should be
236 followed by a final report, unless they are combined into a single submission.
237 However, not all RAE reports will result in a Field Safety Corrective Action (FSCA).

238

7.2 It is advisable to lean towards reporting rather than not reporting in cases of uncertainty regarding the reportability of a RAE.

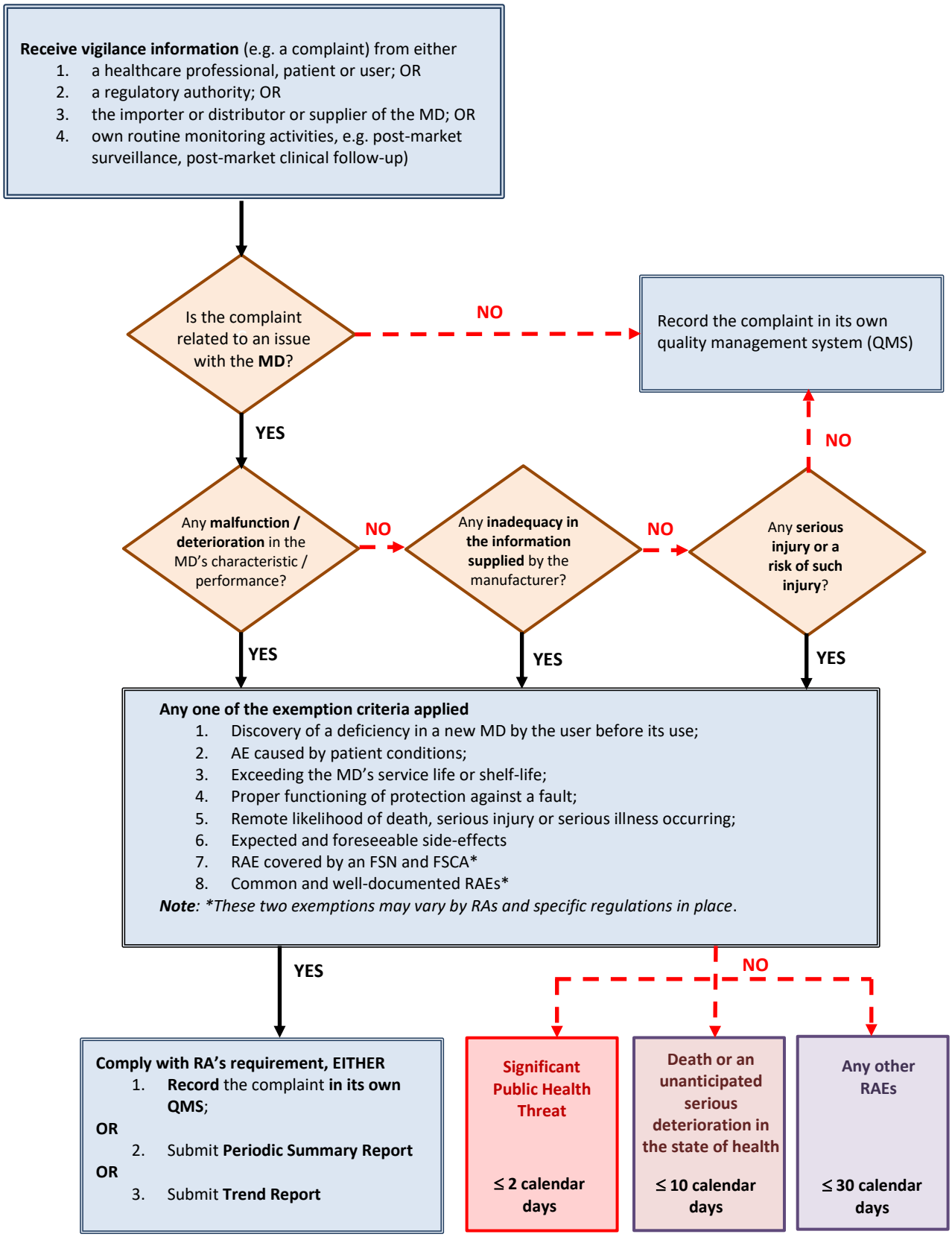
7.3 Manufacturers should notify their ARs, individuals responsible for placing the MDs on the market, and any other authorized agents, such as distributors, about the RAE and FSCA reported under the Vigilance System.

7.4 If the manufacturer is located outside the jurisdiction, a suitable contact point within the jurisdiction should be provided, such as the AR, to act on its behalf for matters related to MD vigilance.

7.5 Any RAE reports should not be unnecessarily delayed due to incomplete information.

7.6 **Flowchart 1** outlines the procedure to be adhered to by MD manufacturer or ARs for handling RAEs.

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



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8. RAE Reporting Requirements for Manufacturer/AR

Step 1: Is the Adverse Event (AE) reportable?

8.1 An AE meeting **ALL** three basic reporting criteria listed below is considered a Reportable Adverse Event (RAE) and must be reported to the relevant RA. Please refer to **Appendix 1** for further elaboration:

(i) An AE has occurred;

AND

(ii) The AE can be classified as RAE, if it has
(1) directly or indirectly resulted in; OR
(2) potential resulted in

a. The death of a patient, user or any other individual; or
b. Serious deterioration in the state of health of patient, user or any other individual; or
c. Likelihood of occurrence of a or b; or
d. A significant public health threat;

AND

(iii) A causal relationship between the RAE and the manufacturer's MD has been established, is reasonable possible or suspected.

Step 2: Does exemption rules apply?

8.2 In certain circumstances, the manufacturer/AR of the MD is not obligated to report the RAE to RAs, but may adhere to trend reporting instead.

8.3 Once the following exemption criteria are met, the RAE 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) RAEs covered by an FSN and FSCA**;

(viii) Common and well-documented RAEs**

Note:

***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 RAE being reported?

8.4 The reporting timeline considers the severity of the RAE. The reporting periods for RAE should be calculated in calendar days, including weekdays, public holidays, Saturdays and Sundays.

8.5 General Rule

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

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

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

(2) RAE resulting **in death or unanticipated serious deterioration in an individual's state of health** must be reported **immediately**[#]**,** and **no later than 10 calendar days** from the awareness of the RAE.

(3) **All other** RAE must be reported **immediately**[#]**,** and **no later than 30 calendar days** from the awareness of the RAE.

Note:

***^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) RAE. If the handing of these RAEs is delegated to an AR or if the manufacturer has outsourced its complaint and RAE management to a subcontractor, then the reference to manufacturer's organization for the awareness date also includes this designated organization.*

*[#]**immediately** refers to without any delay intentionally or negligently caused by the manufacturer.*

8.6 Exceptional Circumstances

(i) **New information affecting initial reportability assessment** – If the manufacturer/AR initially determines that an AE does not meet RAE 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.

8.7 **Table 1** summarizes the RAE reporting timelines

Table 1 Summary of RAE reporting timelines

	Significant public health threat	**Resulting in death or unanticipated serious deterioration in an individual's state of health**	**All other RAEs**
(A) General Rule			
Manufacture Awareness Date - manufacturer/AR is **first made aware of** or **informed** the (potential) RAE, before investigation	Day 0	Day 0	Day 0
Initial Report submission	≤ 2 calendar Days (48 hours)	≤ 10 calendar Days	≤ 30 calendar Days
(B) Exemptional Circumstances – New information affecting initial reportability assessment			
Manufacture Awareness Date - Updated information indicates that AE is reportable	Day 0	Day 0	Day 0
Initial Report submission	≤ 2 calendar Days (48 hours)	≤ 10 calendar Days	≤ 30 calendar Days

Step 4: How to report the RAE?

8.8 To ensure timely reporting, the manufacturer/AR may submit an initial RAE report followed by a subsequent follow-up RAE report. 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.

8.9 The different types of RAE reports are as follows:

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

(ii) **Follow-up report –** This report provides additional information to the initial report, addressing any incomplete information from the initial reporting. The manufacturer/AR must provide a follow-up report to the RA if the investigation exceeds the timeline specified in the initial report.

(iii) **Final report –** This is the last report that the manufacturer/AR intends to submit regarding the RAE. The final report is a written statement detailing the outcome of the investigations and any actions taken.

8.10 **Appendix 3** provides detailed information regarding the RAE reports

9. Periodic Summary Reporting by Manufacturer/AR

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

(i) **RAEs covered by an FSN and FSCA** – RAEs 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 RAEs** – RAEs identified in the MD's risk analysis with corresponding RAE reports reviewed by the manufacturer and relevant RAs. They should be clinically known in terms of root cause and qualitative or quantitative predictability. These RAEs 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

10.1 Trend reporting is initiated when there is a significant rise in the frequency of RAEs that are generally not considered reportable. Specific trigger levels are established to determine when this threshold for reporting is met. 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) **RAEs that have already report:** This includes RAEs covered by an FSN and FSCA, as well as those that are common and have been well-documented; or

(ii) **RAEs that are exempted from reporting**: These are RAEs 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

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 RAEs.

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

11. RAE 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 AR 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 RAE report.

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

12.3 RAE 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 conduct risk assessment of the reported RAE, as deemed relevant.

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.

Appendix 1 – Elaboration of RAE Reporting Criteria

RAE Reporting Criteria	Elaboration
(i) **An AE has occurred**	**(1) Examples of an AE:** a. Malfunction of an MD when used in accordance to the information provided [1], 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[2], 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[3] such as allergic skin reactions like nickel

RAE Reporting Criteria	Elaboration
	allergies or complications in wound therapies.
(ii) The AE can be classified as RAE, if it has **(1) directly or indirectly resulted in; OR** **(2) potential resulted in** **a. The death of a patient, user or any other individual; or** **b. Temporary or permanent serious deterioration in the state of health of patient, user or any other individual; or** **c. A significant public health threat** A serious threat to public health will in principle not be limited to one isolated case or individual patient issue, and identifying these events may depend on signal detection or trending of multiple events of the same nature/typology, same root cause, etc	**(1) RAE indirectly lead to a serious deterioration in the state of health** 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. 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

RAE Reporting Criteria	Elaboration
	(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 RAEs, for example, the distribution of non-sterile MDs falsely labelled as sterile e. Cyberattack targeting life-saving or life-supporting MDs
(iii) A causal relationship between the RAE and the manufacturer's MD has been established, is reasonable possible or suspected.	**(1) Establish causal relationship** When evaluating the connection between their MDs and a RAE, 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 RAE. Therefore, the manufacturer should approach their assessment with caution and refrain from drawing definitive conclusions. If there is uncertainty, the manufacturer must still submit the REA report to RAs.

RAE Reporting Criteria	Elaboration

Notes

[1] ***Malfunction or deterioration in the characteristics or performance of an MD*** *can be defined as a situation where an MD fails to achieve or maintain the performance intended by the manufacturer when used in accordance with the information provided.*

[2] ***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.*

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

456

457 ## **Appendix 2** – Criteria for Non-reportable RAE

458

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 RAE 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*	(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.

Exemption Rules	Examples
information affirming that an MD operated as designed and did not lead to or exacerbate 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	The manufacturer's investigations confirmed an MD was operating as intended, and the RAE 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 RAE 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 *RAE which did not lead to serious deterioration in state of health or death, because a design feature protected against a*	(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.

Exemption Rules	Examples
fault becoming a hazard do not need to be reported. If an alarm system isused, the concept of this system should be generally acknowledge for that type of product	(2) Microprocessor-controlled radiant warmers malfunction and sound an appropriate 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 *RAEs 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 a RAE resulting in death or serious deterioration in state of health occurs, it must be reported, and a reevaluation of the risk is essential. If the reassessment confirms that the risk remains insignificantly low, previous RAEs of the same nature do not needed to be reported retroactively.* *Nevertheless, decisions to omit reporting subsequent failures of a similar nature must be recorded. Any changes in the trend of*	(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
these less severe outcomes, typically an increase, should be reported.	
(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 RAE 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.*	(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

Exemption Rules	Examples
***The factors that contribute to these side effects can be outlined, although numerical prediction may sometimes pose challenges*	

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

REPORTABLE 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 RAE Report		☐ Initial Report ☐ Follow-up Report (Follow-up Number ____) ☐ Combined Initial and Final Report ☐ Final Report
5. Does the RAE represent a significant public health threat? *(Please response to Q6 regardless of whether your answer is affirmative or negative)*		☐ Yes ☐ No

6. Classification of RAE		☐ Death ☐ Unanticipated serious deterioration in state of health ☐ All other reportable RAEs
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 Reportable Adverse Event (RAE)

1. **User Reference Number** *(if applicable)*	
2. Manufacturer/AR awareness date (YYYY/MM/DD)	
3. Date the RAE occurred (YYYY/MM/DD)	
4. Description of the RAE	
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 RAE *(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 RAE, 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 RAE 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.

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

REPORTABLE 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	☐ RAEs covered by an FSN and FSCA **FSN/FSCA Ref. no**.:
	☐ Common and well-documented RAE **Document Ref no.:**
	☐ Others, please specify _____
2. Stage of PSR based on	☐ Observed Failure mode ☐ Root cause
3. Description of RAE 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 RAEs this period**	**Total number RAEs via PSR**	**Total number of RAEs resolved**	**Total number of unresolved RAEs (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.

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

REPORTABLE 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 RAE Trend Report		☐ Trend Initial ☐ Trend Follow-up (Follow-up Number ____) ☐ Trend Final
5. **Does the RAE / 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 RAE 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.