South African Health Products
Regulatory Authority
Building A
Loftus Park
Arcadia
Pretoria

20 November 2023

Guideline for Medical Device Vigilance: Adverse Events Reporting for Licensed Holders

This document has been prepared to serve as a recommendation to a holder of a medical device establishment license (Licensee) / Holder of a Certificate of Registration of a medical device (including an IVD) (HCR) regarding adverse event reporting for medical devices (including IVDs), and the South African Health Products Regulatory Authority (SAHPRA) current thinking on the safety, quality and performance of medical devices. SAHPRA reserves the right to request for any additional information to establish the safety, quality and performance of a medical device (including IVDs) and may make amendments in keeping with the knowledge which is current at the time of consideration of data which has been submitted regarding adverse events for medical devices (including IVDs). SAHPRA is committed to ensure that all medical devices (including IVDs), that are registered are of the required quality, safety and perform as intended. It is important for applicants to adhere to these requirements.

Document History

Final Version	Reason for Amendment	Effective Date
1	– First issue – Industrial comments incorporated – Integration of Recall guideline and Adverse event and post-marketing vigilance guideline for medical devices and IVDs into one guideline – Addition of Annexures 1 & 2 for reporting to Regulatory Authority, and – Published for implementation	August 2015
2	– Updated version following comments received	April 2017
3	Administrative updates: - MCC changed to SAHPRA - Registrar of Medicine changed to Chief Executive Officer	November 2019
4	- Content structured on the new SAHPRA Guideline Template - Previous Guideline no. 8.04 changed to a new document number SAHPGL-MD-03_v4. - Separate Adverse Event Reporting Guideline from Guideline for Recall or Withdrawal of a Medical Device (including IVDs). New Guideline name is Medical Device Vigilance: Adverse Events Reporting for Licensed Holders: SAHPGL-MD-03_v4 New Guideline is based on new medical device regulations. - Include reference to the form for reporting adverse events for medical devices (including IVDs).	March 2023

DR BOITUMELO SEMETE-MAKOKOTLELA
CHIEF EXECUTIVE OFFICER

Contents

Glossary

Abbreviation/ Term	Meaning
Adverse Event	means possible faults or failures of a medical device or IVD or difficulties in the use of or an undesirable outcome associated with the use of a medical device or IVD that can or does result in permanent impairment, injury or death to the professional user or patient user.
Field Safety Corrective Action (FSCA)	an action taken by the holder of a medical device establishment licence ("licensee") and the holder of a certificate of registration (CHR) to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market.
HCR	Holder of Certificate of Registration
IVD	In vitro diagnostic
Near Adverse Event	is an event that might have led to a death or serious injury. It may be that due to the timely intervention of a healthcare practitioner a death or serious injury did not occur. For an event to be defined as a near adverse event, it is sufficient that: • an event associated with the device happened. • if the event occurred again, it might lead to a public health threat, death or serious injury testing or examination of the device or the information supplied with the device, or scientific literature indicated some factor that could lead to a death or serious injury.
Licensee	Holder of a medical device establishment
QMS	Quality Management System
SAHPRA	South African Health Products Regulatory Authority
Serious Injury	(Also known as serious deterioration in state of health) is either: • Life threatening illness or injury. • Permanent impairment of a body function or permanent damage to a body structure. • A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.
Serious public health threat	Any event type, which results in imminent risk of death, serious injury, or serious illness that requires prompt remedial action.
Use Error	Act, or omission of an act, that has a different result to that intended by the manufacturer or expected by the operator.
Vigilance	In relation to a medicine, medical device or IVD, means the continuous monitoring and evaluation of its safety, efficacy and performance profile and the management of any risk throughout its life cycle.

1. INTRODUCTION

This guideline provides a reference document detailing the regulatory requirements for reporting of an adverse event for a medical device (including an IVD) in South Africa and describes the information to be supplied to the South African Health Products Regulatory Authority (SAHPRA). This guideline is intended to holder of a medical device establishment licence (referred to as the "licensee)" and the holder of a certificate of Registration (HCR) in the reporting of an adverse event associated with the use of a medical device (including an IVD).

A medical device (including an IVD) made available for sale in South Africa must meet all the regulatory, safety and performance requirements and any other applicable standards. To improve the monitoring of the performance of a medical device supplied in South Africa, the Regulatory Authority requires the reporting of an adverse event by the licensee and HCR of a medical device (including an IVD).

Whenever there is doubt, the licensee and HCR is advised to report and/or consult SAHPRA for confirmation and/or clarification regarding reporting; refer to the guideline for completing medical device adverse event form for licensed holders.

1.1 Purpose

The purpose of this guideline is to outline the format and data requirements for reporting of adverse events, post- marketing vigilance and monitoring requirements for Medical Devices (including IVDs). This guideline details the requirements for the licensee and HCR to inform the Regulatory Authority of relevant reportable adverse events, within the appropriate timeframes and to also ensure timely and appropriate action is taken.

1.2 Scope

This guideline document is intended as a supplement to the medical device regulations, to aid in the interpretation of the adverse event reporting requirements for a medical device (including an IVD). This guideline is relevant to all medical devices (including IVDs).

This guideline is intended to assist the licensee and HCR of a medical device (including an IVD) in:

- the reporting of an adverse event associated with the use of a medical device (including an IVD),
- the post-marketing vigilance for a medical device (including an IVD) (This includes the management of safety data which arises during post-registration and post-marketing performance and clinical trials), and

- the recall of a medical device (including an IVD) from the marketplace, refer to the current guideline for medical device recalls: *Guideline for Recall or Withdrawal of a Medical Device (including IVDs).*

If there is a problem with a medical device or the way in which it is being used, the licensee and HCR will first conduct an analysis and decide on the appropriate action. One of these actions may require notifying or obtaining further advice from the Regulatory Authority.

Some actions that may need to be taken include:

- follow corrective actions / preventive actions procedures under the manufacturer 's / distributor's quality management system,
- inform the users of the medical device (including an IVD),
- make corrections to the medical device (including an IVD),
- remove, i.e., recall the medical device (including an IVD) from the market.

The Regulatory Authority has established procedures for the ongoing monitoring, vigilance and recall for medical devices (including IVDs) supplied in South Africa.

These guidelines are relevant only to medical devices (including IVDs). Separate guidelines apply to the reporting of adverse events and pharmacovigilance of human medicines including biological and complementary medicines.

2. LEGAL PROVISION

This guideline is based on the requirements of the Medicines and Related Substances Act, (Act 101 of 1965), as amended and the Regulations relating to Medical Devices and *in vitro* diagnostic medical devices (IVDs).

3. VIGILANCE

A well-structured vigilance system is the backbone of a robust regulatory framework to ensure quality and promote the safe use of medical devices (including IVDs). The adverse event reporting provisions in the Regulations are intended to improve monitoring and reduce the recurrence of adverse events related to medical devices (including IVDs) in South Africa, and to ensure that the risk to South Africans of problematic medical devices (including IVDs) is managed appropriately.

3.1 Vigilance Exchange

Through various Mutual Recognition Agreements for medical device (including IVDs) regulation, the Regulatory Authority has an obligation to exchange vigilance information with other national regulatory authorities. Information will be exchanged on adverse events where reportable adverse events, associated with a medical device (including IVDs) that have led or are highly likely to lead to unanticipated serious public health threat and fulfill the following criteria:

Death of a patient, user or other person.

- Serious injury of a patient, user or other person.
- No death or serious injury occurred but the event might lead to death or serious injury of a patient, user or other person if the event recurs. Some jurisdictions refer to these events as near events.
- At the request or other regulatory authorities where corrective action or a recall, is to be taken.
- There is a serious risk to the safety of patients or other users, but where the corrective action is still to be determined.

SAHPRA may share and/or request information from other regulatory authorities about a specific device or class/group of devices concerning:

Adverse events:

- The frequency of the adverse event associated with the device where it is significantly higher than the frequency recorded in the manufacturer's file or significantly higher than the frequency observed with similar devices.
- The event has led or is highly likely to lead to a serious public health threat.
- An increased seriousness or frequency to what was previously reported to the regulatory authority.
- Major deviations regarding the holder of a medical device establishment licence or the holder of a registration certificate’s Quality Management System (QMS).
- Regulatory status changes of a device(s).

The consequences of which:

- have led or are highly likely to lead to serious public health threat, and
- may affect other jurisdictions.

SAHPRA can ask other regulatory authorities about similar experience(s) and what actions were initiated or are being discussed to address the issue, e.g., recalls or Field Safety Corrective Actions (FSCA). SAHPRA will consult the licensee and HCR when preparing a vigilance report to be sent to other regulatory authorities. It is

the responsibility of the licensee and HCR to ensure that the original manufacturer is aware of the Regulatory Authority vigilance report, and that any comments that are made by the original manufacturer are submitted to the Regulatory Authority for consideration.

4. ADVERSE EVENT

4.1 Reportable Adverse Events

Any adverse event that meets the three basic reporting criteria, even if it does not involve a patient or user, should be reported to the Regulatory Authority:

4.1.1. An adverse event has occurred

An adverse event related to a medical device that has led or may lead to mild or moderate or serious threat to public health or death or serious injury, and if one or more of the following events occur but not limited to:

- A malfunction or deterioration in the characteristics or performance;
- An incorrect or out of specification test result;
- The discovery of a design defect during design review;
- An inaccuracy in the labeling, instructions for use and/or promotional materials;
- The discovery of a serious public health threat;
- Inappropriate therapy;
- Unanticipated adverse reaction or unanticipated side effect;
- Use Error;
- Degradation/destruction of the device;
- Interactions with other substances or products;
- False positive or false negative test result falling outside the declared performance of the test;
- Deficiency of a device found by the user prior to its use; and
- Other information becoming available.

4.1.2. The medical device is associated with the adverse event

In assessing the link between the medical device (including an IVD) the event the following should be taken into account:

- The opinion, based on available information, from users and healthcare professionals;
- Information concerning previous, similar events;
- Complaint trends; and
- Other information held by the original manufacturer.

4.1.3. The adverse event has led to the following outcomes:

- Death of a patient or user
- A serious injury
- A near adverse event.

It is possible that the reporter will not have enough information to decide on the reportability of an adverse event. In such a case, the reporter should make reasonable efforts to obtain additional information to aid in the decision. Where applicable, the reporter should consult with the healthcare professional involved and make all reasonable efforts to retrieve the medical device for evaluation.

The event is considered "adverse" if in the case of reoccurrence, it could lead to death or serious injury. This applies also if the examination of the device or a deficiency in the information supplied with the device, or any information associated with the device, indicates some factor which could lead to an event involving death or serious injury.

NOTE: Refer to the decision tree related to evaluating the reportability of an adverse event (Appendix 1).

4.2 Reporting an adverse event associated with a Medical Device (including an IVD)

The reporting requirements for the Authorised Representative of the licensee and HCR are a condition of sale of a medical device (including an IVD) in South Africa. Breaching conditions may lead to suspension or cancellation of the sale of the medical device as well as constituting an offence. The Authorised Representative of the licensee and HCR is responsible for forwarding reports of all adverse events to the original manufacturer for assessment under the original manufacturers surveillance systems.

It is possible that the licensee and HCR will not have enough information to decide if the problem should be reported to the Regulatory Authority. The Authorised Representative of the licensee and HCR should make reasonable efforts to obtain additional information to assist in making this decision. A record of decisions made (with supporting documentation) must be retained by the licensee and HCR.

In assessing the link between the device and the event, the Authorised Representative of the licensee and HCR should take into account:

- the opinion, based on available information, from a healthcare professional,
- information concerning previous, similar events,

- other information held by the Authorised Representative of the licensee and HCR.

In complex situations, it should be assumed that the medical device was associated with the event. If there is any doubt about whether a report should be submitted, the report should be submitted.
Where possible, the Authorised Representative of the licensee and HCR should consult with the user and/or healthcare professional(s) or health facilities involved and do their utmost to retrieve the medical device for purposes of inspection where possible.

4.2.1 Examples of Reportable Adverse Events

- The premature revision of an orthopaedic implant due to loosening or fracture.
- An infusion pump stops, due to a malfunction, but fails to give an alarm. The patient receives an under-infusion of needed fluids.
- During the use of an external defibrillator on a patient, the defibrillator failed to deliver the programmed level of energy due to a malfunction.
- An intravenous set separates and the comatose patient's blood leaks onto the floor, resulting in significant blood loss.

4.2.2 Examples of Reportable Adverse Events Involving Public Health Concerns

- Fatigue testing performed on a commercialised heart valve bioprosthesis demonstrates premature failure, which would indicate that a risk to public health could occur.
- After delivery of an orthopaedic implant, errors were discovered in heat treatment records raising questions about the effectiveness of the implant's materials that would create a risk to public health.

In certain circumstances it is not necessary to report an adverse event to SAHPRA – refer to section 4.3 below. Where exemption is not applicable, only an adverse event that occurs in South Africa must be reported to the Regulatory Authority. Any remedial or corrective action that arises outside of South Africa for a medical device that is also supplied in South Africa should be held in the records of the licensee and be available to SAHPRA on request.

Adverse events for medical devices (including IVDs) that occur outside of South Africa for medical devices (including IVDs) also supplied in South Africa do not need to be reported to the Regulatory Authority, however, records of these events should be available if requested.

4.3 Exemption from Reporting an Adverse Event to the Regulatory Authority

There are eight exemption rules that can apply (see Appendix 3: table of exemption rules). However, these rules do NOT apply when:

- a medical device (including an IVD), event or issue specifically identified by the Regulatory Authority as an issue that requires close monitoring— the affected licensee(s) and the HCR will be notified by the Regulatory Authority when this occurs;
- an adverse event normally subject to a reporting exemption, where a change in trend (usually an increase in frequency) or pattern is identified;
- adverse events associated with use error, as the Regulatory Authority may use this data to identify trends with similar products that may lead to recommendations for:
    - corrective action for the device
    - revising the labelling or *Instructions for Use*
    - identifying a need for increased user education.

If a licensee and HCR believes an exemption rule applies to reporting an adverse event, the reasons for not reporting the event should be documented and retained on record.

4.4 Timeframes for submitting an adverse event report to SAHPRA

The period in which the Authorised Representative of the licensee and HCR must give information to the Regulatory Authority is:

4.4.1 if the information relates to an event or other occurrence that represents a serious threat to public health - **48 hours** after the person becomes aware of the event or occurrence; and

4.4.2 if the information relates to an event or other occurrence that led to the death, or a serious deterioration in the state of health, of a patient, a user of the device, or another person – **10 calendar days** after the person becomes aware of the event or occurrence; and

4.4.3 If the information relates to an event or other occurrence a recurrence of which might lead to the death, or a serious deterioration in the state of health, of a patient, a user of the device, or another person - **30 days** after the person becomes aware of the event or occurrence.

4.5 Timeframes for submitting clinical studies adverse event report to SAHPRA

4.5.1 **In clinical studies**, report serious adverse events which have been determined to represent a serious health threat to the study population must be reported by the sponsor within **48 hours** following the determination that the serious health threat exists.

4.5.2 **In clinical studies**, report within **10 calendar days** after becoming aware the following; Unanticipated Serious Adverse Device Effect and serious adverse event, adverse event resulting in death, or resulting in a serious deterioration in the health of the subject that either: adverse event resulted in a life-threatening illness or injury, adverse event resulted in a permanent impairment of a body structure or a body function and serious adverse event, other than unanticipated serious adverse device effect(s) that have led to foetal distress, foetal death or a congenital abnormality or birth defect

4.5.3 **In clinical studies**, report within **30 days**; serious adverse event other than unanticipated serious adverse device effect, resulting in a serious deterioration in the health of the subject that either: required in-patient hospitalization or prolongation of existing hospitalization, adverse event resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function. Any device deficiency that might have led to a serious adverse event if either: suitable action had not been taken; intervention had not been made; or circumstances had been less fortunate.

If, after becoming aware of a potentially reportable adverse event, there is uncertainty about whether the event is reportable, the sponsor must submit a report within the timeframe required for that type of event.

4.6 Adverse event reporting

The adverse event form should be submitted as per timelines and include one of the following report types with the following information:

4.6.1. **Initial report:** defined as the first information submitted by the holder of the medical device establishment licence (as per Section 22C of the Medicines Act 101 of 1965 as amended) (referred to as a “licensee”) and HCR about a reportable event, but the information may be incomplete and supplementary information will need to be submitted. This includes immediate notification.

4.6.2. **Follow-up report:** defined as a report that provides supplemental information about a reportable event that was not previously available).

4.6.3. **Final report:** defined as the last report that the licensee and HCR expect to submit about the reportable event. A final report may also be the first report or the follow-up report depending on the information available

For details to be included in an adverse event report, refer to the *Guideline for completing an adverse event report form for licensed holders.*

The report submitted to SAHPRA should be dated and signed by the Authorised Representative and should not be unduly delayed if the information is incomplete, a follow-up report should be submitted as soon as it is available. It is important to get this process underway as additional information can be provided later.

4.7 Access to medical devices involved in an adverse event

Where possible, the Authorised Representative of the licensee and HCR should consult with the user of the medical device about the event before a report is submitted to the Regulatory Authority. The licensee and HCR may also wish to have access to the medical device involved in the event to help decide whether the event should be reported to the Regulatory Authority. Such access would be at the discretion of the user or healthcare facility concerned, but they are advised to assist the licensee and HCR to determine the root cause of the event. All precautions required for the transportation of biohazardous materials should be undertaken and medical device (including IVD) kits with biohazardous packaging should be used.

If the licensee and HCR has access to the medical device and cannot transport the used medical device without cleaning or decontamination process which may involve altering the device in a way that may affect subsequent analysis, the HCR / licensed manufacturer / licensed distributor should, through the Authorised Representative, inform the Regulatory Authority as part of its report.

The outcome of any investigation may include one or more:

- referral to other areas of the Regulatory Authority for regulatory actions, such as auditing of the manufacturer.
- implementation of a Field Safety Corrective Action relating to the affected medical device (including an IVD) might lead to the following actions (For further information Refer to the *Guideline for Recall or Withdrawal of a Medical Device (including IVDs*):

- recall the type of medical device (including IVD) from the market and prevent further sale of such medical device (including IVD) until written approval by SAHPRA to do so.
- withdraw the affected medical device (including an IVD) from supply in South Africa.
- allow correction at the user's site following issue of a Safety Alert where there is a need to reinforce the manufacturer's *Instructions for Use* to those responsible for the use of the medical device or those affected by the problem.

- product improvement for problems that are not safety-related - carried out by the manufacturer report on the Regulatory Authority website and/or appropriate communication.

4.8 How to report an adverse event

A reportable medical device adverse event (including an IVD) should be reported to SAHPRA's Medical Device unit on the dedicated email address: mdvigilance@sahpra.org.za

5. REFERENCES

The following related documents are referenced:

1. Act 101 of 1965 Medicines and Related Substances Act, as amended

2. Regulations relating to Medical Devices. Government Notice No. **1515**, Government Gazette No. 40480 09 December 2016

3. GHTF/SG2/N54R8:2006 Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices

4. GHTF/SG2/N87:2012 Medical Devices: Post Market Surveillance: An XML Schema for the electronic transfer of adverse event data between manufacturers, authorized representatives and National Competent Authorities

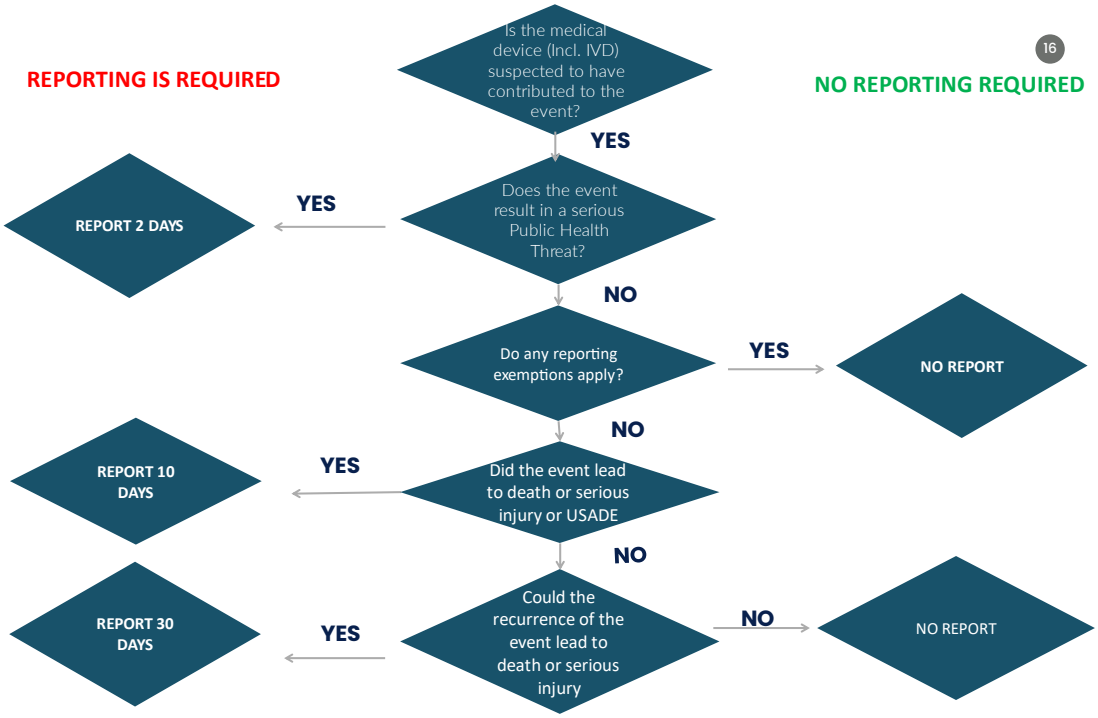
5. GHTF/SG5/N5:2012 Reportable Events During Pre-Market Clinical Investigations

6. IMDRF IMDRF/AE WG/N43FINAL:2020 IMDRF terminologies for categorized Adverse Event Reporting (AER): terms, terminology structure and codes

6. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the previous Guideline: 8.04 Recall, Adverse Event and Post-Marketing Vigilance Reporting of Medical Devices and IVDs and is divided into two guidelines with a new document number SAHPGL-MD-03_v4. It will be reviewed on this timeframe or as and when required.

Appendix 1: Decision Tree Flow Chart for Adverse Event Reporting



Appendix 3: Table of Adverse Event Reporting Exemption Rules and Examples

Rule No.	Exemption Rule	Examples of adverse events exempt from reporting
1	▪ Deficiency of a new device found by the user prior to its use regardless of the existence of provisions in the Instruction for Use provided by the manufacturer, deficiencies of devices that will be always detected by the user and where no serious injury has occurred, do not need to be reported. *Please note: If the device is used the exemption does not apply—the event must be reported*.	▪ A user performs an inflation test (standard procedure) prior to inserting the balloon catheter in the patient as required in the *Instructions for Use* accompanying the device. Malfunction on inflation is identified. Another balloon is used. Patient is not injured. ▪ Sterile single-use device packaging is labelled with the caution '*do not use if package is opened or damaged*'. Open package seals are discovered prior to use, and the device is not used. ▪ An intravenous administration set tip protector has fallen off the set during distribution resulting in a non-sterile fluid pathway. The intravenous administration set was not used.
2	▪ Adverse event caused solely by patient conditions ▪ When the manufacturer has information that the root cause of the adverse event is due to patient condition, the event does not need to be reported. These conditions could be pre-existing or occurring during device use. ▪ To justify not reporting, the manufacturer should have information available to conclude that the device performed as intended and did not cause or contribute to a death or serious injury. A person qualified to make a medical judgement would accept the same conclusion.	▪ An orthopaedic surgeon implants a hip joint and warns against sports-related use. Patient chooses to go water skiing and subsequently requires premature revision. ▪ The early revision of an orthopaedic implant due to loosening caused by the patient developing osteoporosis. ▪ A patient died after dialysis treatment. The patient had end- stage-renal disease and died of renal failure.
3	▪ Service life of the medical device ▪ The service life is defined as '*the time or usage that a device is intended to remain functional after it is manufactured, placed into use, and maintained as specified*'. The service life must be specified by the device manufacturer and included in the master record (technical file). ▪ When the only cause for the adverse event was that the device exceeded its service life and the failure mode is not	▪ Loss of sensing after a pacemaker has reached its end of life. The elective replacement indicator has shown up in due time according to the device specification. Surgical explanation of pacemaker is required. ▪ A drill bit was used beyond the end of its specified life. It fractured during invasive operation. Operation time was prolonged due to the difficulty to retrieve the broken parts.

	unusual, the adverse event does not need to be reported. ▪ Assessment of whether an event is exempt from reporting under this rule must be based on the information in the master record, on the label or in *Instructions for Use* for the device.	

4	▪ Protection against a fault functioned correctly ▪ Adverse events that did not lead to serious injury or death, because a design feature protected against a fault becoming a hazardous situation (in accordance with relevant standards or documented design inputs) do not need to be reported.	▪ An infusion pump stops, due to a malfunction, but gives an appropriate alarm (for example, in compliance with relevant standards) and there was no injury to the patient. ▪ Microprocessor-controlled radiant warmers malfunction and provide an audible appropriate alarm, in compliance with relevant standards and there was no injury to the patient. ▪ During radiation treatment, the automatic exposure control is engaged, and the treatment stops. Although the patient receives less than an optimal dose, the patient is not exposed to excess radiation.
5	▪ Remote likelihood of occurrence of death or serious injury ▪ Adverse events that could lead, but have not yet led, to death or serious injury, but have a remote likelihood of causing death or serious injury, and which have been established and documented as acceptable after risk assessment do not need to be reported. ▪ If an adverse event resulting in death or serious injury occurs, the adverse event is reportable, and a reassessment of the risk is necessary. If reassessment determines that the risk remains remote, previous reports of near events of the same type do not need to be reported retrospectively. Decisions not to report subsequent failures of the same type must be documented. ▪ Please note: A change in the trend (usually an increase in frequency) of these non-serious outcomes must be reported.	▪ The manufacturer of a pacemaker supplied to the market identified a software bug and determined that the likelihood of occurrence of a serious injury with a particular setting is remote. No patients experienced any adverse health effects. ▪ The manufacturer of blood donor sets obtains repeated complaints of minor leaks of blood from these sets. No patient injuries from blood loss or infections of staff have been reported. The chance of infection or blood loss has been re-evaluated by manufacturer and deemed remote.
6	▪ Expected and foreseeable side effects that are documented in manufacturer's Instructions for Use or labelling ▪ Side effects that are clearly identified in the manufacturer's labelling or are clinically well known as being foreseeable and having a certain functional or numerical predictability when the device was used as	▪ A patient receives a second-degree burn during the use of an external defibrillator in an emergency. The risk assessment documents that such a burn has been accepted in view of the potential patient benefit and a warning is provided in the *Instructions for Use*. The frequency of burns is occurring within range specified in the device master record. ▪ A patient has an undesirable tissue reaction that is previously known and documented in the device master record. ▪ A patient who has a mechanical heart valve developed endocarditis ten years after implantation

	intended need not be reported. ▪ Some of these events are well known in the medical, scientific, or technology fields. Others may have been clearly identified during clinical investigation and labelled by the manufacturer. ▪ Documentation, including the risk assessment, for the particular side effect should be available in the device master record prior to the occurrence of adverse events. The manufacturer cannot conclude in the face of events that they are foreseeable unless there is prior supporting information.	and then died. ▪ Placement of central line catheter results in an anxiety reaction and shortness of breath. Both reactions are known and labelled side effects.
7	▪ Adverse events described in an advisory notice ▪ Adverse events that occur after the manufacturer has issued an advisory notice need not be reported individually if they are specified in the notice. Advisory notices include removals from the market, corrective actions, and product recalls. The manufacturer should provide a summary report, the content and frequency of which should be agreed with the Regulatory Authority.	▪ A manufacturer issued an advisory notice and undertook a recall of a coronary stent that migrated due to inadequate inflation of an attached balloon mechanism. Subsequent examples of stent migration were summarised in quarterly reports required for the recall action and individual adverse events did not have to be reported.
8	▪ Reporting exemptions granted by the Regulatory Authority ▪ Upon request by the applicant, common and well-documented events may be exempted by the Regulatory Authority from reporting or changed to periodic reporting on a case-by-case basis.	

Appendix 4: Examples of an Adverse Event that is a threat to Public Health.

- Fatigue testing performed on a commercialised heart valve bio prosthesis demonstrates premature failure, which would indicate that a risk to public health could occur.
- After delivery of an orthopaedic implant, errors were discovered in the heat treatment records raising questions about the effectiveness of the implant's materials that would create a risk to public health.
- A manufacturer provides insufficient details on cleaning methods for reusable surgical instruments used in brain surgery, despite the obvious risk of transmission of Creuzfeld-Jacob Disease (CJD).
- A manufacturer suspects risk of Bovine Spongiform Encephalopathy (BSE) cross contamination from materials of animal or biological origin that could result in progressively degenerative neurological diseases known as transmissible spongiform encephalopathies (TSEs).

Appendix 5: Examples of Reportable Adverse Events

- The premature revision of an orthopaedic implant due to loosening or fracture.
- An infusion pump stops, due to a malfunction, but fails to give an alarm. The patient receives an under-infusion of needed fluids.
- During the use of an external defibrillator on a patient, the defibrillator failed to deliver the programmed level of energy due to a malfunction.
- An intravenous set separates and the comatose patient's blood leaks onto the floor, resulting in significant blood loss.
- Loss of sensing after a pacemaker has reached end of life. Elective replacement indicator did not show up in due time, although it should have according to device specification.

  On an X-ray vascular system during patient examination, the C arm had uncontrolled motion. The patient was hit by the image intensifier and his nose was broken. The system was installed, maintained, and used according to manufacturer's instructions.

  * It was reported that a monitor suspension system fell from the ceiling when the bolts holding the swivel joint broke off. Nobody was injured in the surgical theatre at that time, but a report is necessary (near event). The system was installed, maintained, and used according to manufacturer's instructions.

  * Sterile single use device packaging is labelled with the caution 'do not use if package is opened or damaged'. The label is placed by incorrect design on inner packaging. Outer package is removed but device is not used during procedure. Device is stored with inner packaging only which does not offer a sufficient sterile barrier.

  * A batch of out-of-specification blood glucose test strips is released by manufacturer. Patient

uses strips according to instructions, but readings provide incorrect values leading to incorrect insulin dosage, resulting in hypoglycaemic shock and hospitalization.

* Premature revision of an orthopaedic implant due to loosening. No cause yet determined.
* An infusion pump stops, due to a malfunction, but fails to give an alarm. Patient receives under-infusion of needed fluids and requires extra days in hospital to correct.
* Manufacturer of a pacemaker released on the market identified a software bug. Initial risk assessment determined risk of serious injury as remote. Subsequent failure results in new risk assessment by manufacturer and the determination that the likelihood of occurrence of a serious injury is not remote. Medical Devices: Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices – GHTF/SG2/N54R8:2006 Study Group 2 Final Document 30 November 2006 Page 9 of 37
* Patients undergoing endometrial ablation of the uterus suffered burns to adjacent organs. Burns of adjacent organs due to thin uterine walls were an unanticipated side effect of ablation. * Manufacturer does not change ablation device label and fails to warn of this side effect which may be produced when the device is working within specification.
* Healthcare professional reported that during implant of a heart valve, the sewing cuff is discovered to be defective. The valve was abandoned, and a new valve was implanted and pumping time during surgery was extended.
* During the use of an external defibrillator on a patient, the defibrillator failed to deliver the programmed level of energy due to malfunction. Patient died.
* An intravenous set separates, the comatose patient's blood leaks onto the floor, the patient bleeds to death.
* Unprotected ECG cable plugged into the main electricity supply – patient died.
* Fatigue testing performed on a commercialized heart valve bio prosthesis demonstrates premature failure, which resulted in risk to public health.
* After delivery of an orthopaedic implant, errors were discovered in heat treatment records leading to non-conforming material properties, which resulted in risk to public health.
* Testing of retained samples identified inadequate manufacturing process, which may lead to detachment of tip electrode of a pacemaker lead, which resulted in risk to public health.
* Manufacturer provides insufficient details on cleaning methods for reusable surgical instruments used in brain surgery, despite obvious risk of transmission of CJD.