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

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The document herein was produced by the Global Harmonization Task Force, a voluntary group of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide *non-binding* guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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

Introduction

The objective of the adverse event reporting and subsequent evaluations is to improve protection of the health and safety of patients, users and others by disseminating information which may reduce the likelihood of, or prevent repetition of adverse events, or alleviate consequences of such repetition.

This document has been created by the Global Harmonization Task Force Study Group 2: Medical Device Vigilance/Post Market Surveillance. Study Group 2 is made up of representatives of the regulatory authorities of the USA, Europe, Canada, Japan and Australia as well as European, US, Canadian and Japanese industry representatives.

For the purpose of this document, the term "manufacturer" must be understood as including the manufacturer, its authorized representative or any other person who is responsible for placing the device on the market.

The existing regulatory requirements of the participating countries involved in SG2 require medical device manufacturers to notify NCAs of certain adverse events.

This document represents a global model, which provides guidance on the type of adverse events associated with medical devices that should be reported by manufacturers to a National Competent Authority (NCA). It has been elaborated on the basis of the regulatory requirements existing in the participating member countries.

The information and guidance contained herein represents a model, which may not reflect current regulatory requirements. Even if the present reporting criteria of the participating countries are very similar, they are not identical. This document provides a future model towards which those existing systems should converge. The principles laid down in this document should be considered in the development or amendment of regulatory systems in the participating countries or other countries.

In order to improve the monitoring of the performance of medical devices placed on their market, NCA should encourage the reporting of adverse events by the users. Such reports may be addressed either directly to the NCA, or to the manufacturer, or to both depending on national practices. Where the user informs directly the NCA about an event the NCA should adopt administrative measures to ensure that the pertinent manufacturer is informed without delay of such a notification.

NCAs may require certain adverse events to be reported as soon as possible for public health reasons. In such cases, the report may not contain complete information and should be followed up with a complete report.

The act of reporting an event to a NCA is not to be construed as an admission of manufacturer, user, or patient liability for the event and its consequences. Submission of an adverse event report does not, in itself, represent a conclusion by the manufacturer

that the content of this report is complete or confirmed, that the device(s) listed failed in any manner. It is also not a conclusion that the device caused or contributed to the adverse event. It is recommended that reports carry a disclaimer to this effect.

It is possible that the manufacturer will not have enough information to decide definitely on the reportability of an event. In such a case, the manufacturer should make reasonable efforts to obtain additional information to decide upon reportability. Where appropriate, the manufacturer should consult with the medical practitioner or the health-care professional involved, and do his utmost to retrieve the concerned device.

NCAs for medical devices usually have, or are part of larger organizations, which have, a responsibility for the protection of public health. To perform their duties they need information, on a voluntary basis if no regulatory requirement exists, about events coming to the notice of manufacturers which might have relevance to the public health but which are not harmonized under the guidelines set out in this document, e.g. use error. Such notifications might fall outside the national adverse event reporting system and could be made in confidence and with suitable anonymity, depending on respective provisions by the responsible NCA.

As a general principle, there should be a pre-disposition to report rather than not to report in case of doubt on the reportability of an event.

1 Decision process

Any event which meets the three basic reporting criteria listed in sections 1.1 through 1.3 below is considered as an adverse event and should be reported to the relevant NCA.

Reporting may be exempted if any one of the exclusion rules listed in section 2 below is applicable.

> However those adverse events involving particular issues of public health concern as determined by the relevant NCA should be reported regardless of exemption criteria (see 1.1.d).
>
> Similarly those adverse events which are subject to an exemption become reportable to the NCA if a change in trend (usually an increase in frequency) or pattern is identified.

Specific rules apply to events involving use error and can be found in section 3.

1.1 *An event has occurred*

The manufacturer becomes aware of information regarding an event which has occurred with its device.

This also includes situations where testing performed on the device, examination of the information supplied with the device or any scientific information indicates some factor that could lead or has lead to an event.

Typical events are:

a) A malfunction or deterioration in the characteristics or performance.

A malfunction or deterioration should be understood as a failure of a device to perform in accordance with its intended purpose when used in accordance with the manufacturer's instructions.

The intended purpose means the use for which the device is intended according to the data supplied by the manufacturer on the labeling, in the instructions and/or in promotional materials.

b) An inadequate design or manufacture.

This would include cases where the design or manufacturing of a device is found deficient.

c) An inaccuracy in the labeling, instructions for use and/or promotional materials.

Inaccuracies include omissions and deficiencies.

Omissions do not include the absence of information that should generally be known by the intended users.

d) A significant public health concern.

This can include an event that is of significant and unexpected nature such that it becomes alarming as a potential public health hazard, e.g. human immunodeficiency virus (HIV) or Creutzfeldt-Jacob Disease (CJD).

These concerns may be identified by either the NCA or the manufacturer.

e) Other information becoming available.

This can include results of testing performed by the manufacturer on its products, or by the user prior to being used on the patient, or by other parties.

This can also include information from the literature or other scientific documentation.

1.2 ***The manufacturer's device is associated with the event.***

In assessing the link between the device and the event, the manufacturer should take into account:

- The opinion, based on available information, from a healthcare professional;
- Information concerning previous, similar events;
- Other information held by the manufacturer.

This judgement may be difficult when there are multiple devices and drugs involved. In complex situations, it should be assumed that the device was associated with the event.

1.3 ***The event led to one of the following outcomes***:

1.3.1 ***Death of a patient, user or other person.***

1.3.2 ***Serious injury of a patient, user or other person.***

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.

The interpretation of the term "serious" is not easy, and should be made in consultation with a medical practitioner when appropriate.

The term “permanent” means irreversible impairment or damage to a body structure or function, excluding minor impairment or damage.

Medical intervention is not in itself a serious injury. It is the reason that motivated the medical intervention that should be used to assess the reportability of an event.

1.3.3 ***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 incidents.

All events do not lead to a death or serious injury. The non-occurrence of such a result might have been due to circumstances or to the timely intervention of health care personnel.

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.

Examples of Reportable Adverse Events

*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 theater at that time but a report is necessary (near incident). The system was installed, maintained, and used according to manufacturer's instructions.

*Sterile single use device packaging is labeled 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 hypoglycemic shock and hospitalization.

* Premature revision of an orthopedic 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.

* 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 bioprosthesis demonstrates premature failure, which resulted in risk to public health.

* After delivery of an orthopedic 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.

2 Exemption rules.

Whenever any one of the following exemption rules is met, the adverse event does not need to be reported to NCA by the manufacturer.

2.1 *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 would normally be detected by the user and where no serious injury has occurred, do not need to be reported.

Examples of non reportable adverse events:

* User performs an inflation test 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 labeled with the caution *'do not use if package is opened or damaged'.* Open package seals are discovered prior to use, device is not used.

*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.

2.2 *Adverse event caused 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 preexisting or occurring during device use.

To justify no report, the manufacturer should have information available to conclude that the device performed as intended and did not cause or contribute to death or serious injury. A person qualified to make a medical judgement would accept the same conclusion.

Examples of non reportable adverse events:

* Orthopedic surgeon implants a hip joint and warns against sports-related use. Patient chooses to go water skiing and subsequently requires premature revision due to not following directions.

* Early revision of an orthopedic 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.

2.3 *Service life of the medical device.*

When the only cause for the adverse event was that the device exceeded its service life as specified by the manufacturer and the failure mode is not unusual, the adverse event does not need to be reported.

The service life must be specified by the device manufacturer and included in the master record [technical file] or, where appropriate, the instructions for use (IFU). 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. Reporting assessment shall be based on the information in the master record or in IFU.

Reporting of adverse events related to the reuse of devices labeled for single use (or labeled “for single use only”) is handled under Section 3: Use Error.

Examples of non-reportable adverse events:

*Loss of sensing after a pacemaker has reached end of life. Elective replacement indicator has shown up in due time according to device specification. Surgical explantation of pacemaker required.

* A drill bit was used beyond end of specified life. It fractured during invasive operation. Operation time was prolonged due to the difficulty to retrieve the broken parts.

2.4 *Protection against a fault functioned correctly.*

Adverse events which did not lead to serious injury or death, because a design feature protected against a fault becoming a hazard (in accordance with relevant standards or documented design inputs), do not need to be reported.

Examples of non-reportable adverse events:

*An infusion pump stops, due to a malfunction, but gives an appropriate alarm (e.g. in compliance with relevant standards) and there was no injury to the patient.

*Microprocessor-controlled radiant warmers malfunction and provide an audible appropriate alarm. (e.g., in compliance with relevant standards) and there was no injury to the patient.

* During radiation treatment, the automatic exposure control is engaged. Treatment stops. Although patient receives less than optimal dose, patient is not exposed to excess radiation.

2.5 *Remote likelihood of occurrence of death or serious injury.*

Adverse events which 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 risk remains remote, previous reports of near incidents of the same type do not need to be reported retrospectively. Decisions not to report subsequent failures of the same type must be documented. Note that change in trend of these non-serious outcomes must be reported as specified in Section 1.

Examples of non-reportable adverse events:

* Manufacturer of pacemaker released on 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 adverse health effects.

* Manufacturer of blood donor sets obtains repeated complaints of minor leaks of blood from these sets. No patient injury from blood loss or infections of staff have been reported. Chance of infection or blood loss has been reevaluated by manufacturer and deemed remote.

2.6 *Expected and foreseeable side effects.*

Side effects which are clearly identified in the manufacturer's labeling or are clinically well known as being foreseeable and having a certain functional or numerical predictability when the device was used as intended need not be reported.

Some of these events are well known in the medical, scientific, or technology field; others may have been clearly identified during clinical investigation and labeled by the manufacturer.

Documentation, including risk assessment, for the particular side effect should be available in the device master record prior to the occurrence of adverse events: manufacturer can not conclude in the face of events that they are foreseeable unless there is prior supporting information.

Examples of non-reportable adverse events

* A patient receives a second-degree burn during the use in an emergency of an external defibrillator. Risk assessment documents that such a burn has been accepted in view of potential patient benefit and is warned 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 (e.g. nickel allergy) previously known and documented in the device master record.

* Patient who has a mechanical heart valve developed endocarditis ten years after implantation and then died.

* Placement of central line catheter results in anxiety reaction and shortness of breath. Both reactions are known and labeled side effects.

2.7 *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 relevant NCA.

Example of non-reportable adverse events

* Manufacturer issued an advisory notice and recall of a coronary stent that migrated due to inadequate inflation of an attached balloon mechanism. Subsequent examples of stent migration were summarized in quarterly reports concerning the recall action and individual adverse events did not have to be reported.

2.8 *Reporting exemptions granted by NCA.*

Common and well-documented events may be exempted by NCA from reporting or changed to periodic reporting upon request by the manufacturer.

3 Use error

The reportability of adverse events involving use error is not globally harmonized. Reportability is subject to regulatory requirements of the relevant NCA.

The term use error covers unintentional and intentional misuse.

Some jurisdictions may require reporting of adverse events involving use error even though the events did not occur in their own jurisdiction.

NCAs generally prefer to receive use error reports, especially those involving death or serious injury.

The reprocessing and re-use of devices labeled by the manufacturer for single use (“single use only”) is a common practice. However, since this is clearly outside the intended use of the device as stated by the manufacturer, reports of adverse events potentially associated with reuse should be treated as reports of use error.

Similarly, adverse events due to the use of any device for clinical situations not intended by the manufacturer (also called “off label” use) should be treated similar to use error.