

PROPOSED DOCUMENT

Global Harmonization Task Force

Title: Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices

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Preface

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.

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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 and industry representatives of the USA, Europe, Canada, Japan and Australia.

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.

This document is a consolidation of final GHTF guidance on Adverse Event Reporting. It was produced by combining GHTF/SG2/N21 Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative with the requirements from the following documents:

- GHTF/SG2/N31 Proposal for Reporting of Use Errors with Medical Devices by their Manufacturer or Authorized Representative,
- GHTF/SG2/N32 Universal Manufacturer Report Form,
- GHTF/SG2/N33 Timing of Adverse Event Reports,
- GHTF/SG2/N36 Manufacturers Trend Reporting of Adverse Events.

For reference purposes the complete copies of these documents have been included in the appendices.

1.0 Scope

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, NCAs 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 the NCA directly 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.

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.

2.0 Definitions

Immediate adverse event report: For purposes of adverse event reporting, immediately means as soon as possible, but not later than 10 elapsed calendar days following the date of awareness of the event.

Serious public health threat: Any event type, which results in imminent risk of death, serious injury, or serious illness that may require prompt remedial action.

Unanticipated death or unanticipated serious injury: A death or serious injury is considered unanticipated if the condition leading to the event was not considered in a risk analysis performed during the design and development phase of the device. There must be documented evidence in the design file that such analysis was used to reduce the risk to an acceptable level.

Use error: Act, or omission of an act, that has a different result to that intended by the manufacturer or expected by the operator. Use error includes slips, lapses, mistakes and reasonably foreseeable misuse. Definition taken from AAMI HE 74:20012 and IEC/CD2 60601-1-6:20023. See also Appendix D for examples of potential use errors.

3.0 Decision Process

Any event which meets the three basic reporting criteria listed in sections 3.1 through 3.3 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 4, 5.1.2 and 5.2 below are 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 3.1.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. See Appendix C for information.

3.1 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) Use Error (for details see section 5)
- f) Any other information that becomes 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, other scientific documentation or increase in trend (see appendix C)

3.2 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 judgment 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.

3.3 The Event Led to One of the Following Outcomes:

3.3.1 Death of a Patient, User or Other Person.

3.3.2 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.

3.3.3 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.

Include relevant information that might impact the understanding or evaluation of the adverse event AND that is not included elsewhere in this report. For example- "the patient was confused prior to becoming trapped in the bedsides"; "the patient was a very low birth weight premature delivery and had a central line placed three days before onset of cardiac tamponade"; "the X-ray machine was over 20 years old and had been poorly maintained at the time of the adverse event"; etc

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 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 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.

4.0 Exemption Rules

Whenever exemption rules 4.1-4.6 and 4.8(a) are met, the adverse event does not need to be reported to the NCA by the manufacturer. Whenever exemption rules 4.7 or 4.8 (b) are met, the manufacturer will need to submit periodic or summary reports in lieu of individual adverse event reports.

Note: See Section 5, which also includes an exemption on use error and a consideration for handling abnormal use.

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. See Appendix C for information.

4.1 Deficiency of a Device Found by the User prior to patient use.

Deficiencies of devices that would always be detected by the user and where no serious injury has occurred do not need to be reported.

Based on the information stated, these are 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. A malfunction on inflation is detected. 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 detected 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. Since the fault was detected the intravenous administration set was not used.

4.2 Adverse Event Caused by Patient Conditions.

When the manufacturer has information that the root cause of the adverse event is due to a patient's 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 judgment would accept the same conclusion.

Examples of non-reportable adverse events:

* 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.

* The death of a patient that is unrelated to any implanted device or device used to treat the patient.

4.3 Service Life or Shelf Life of the Medical Device.

When the only cause for the adverse event was that the device exceeded its service life or shelf 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 or shelf life must be specified by the device manufacturer in the product labeling or instructions for use. Service life or shelf 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.

NOTE: Reporting of adverse events related to the reuse of devices labeled for single use (or labeled "for single use only") is handled under Section 5: Use Error.

Examples of non-reportable adverse events:

*Loss of sensing after a pacemaker has reached its expected end of life as indicated in the instructions for use. Elective replacement indicator has shown up in due time according to device specification. Surgical explantation of pacemaker required.

* Surgical glove was used after expiry date. User was exposed to infected blood due to glove failure.

4.4 Malfunction¹ Protection Operated Correctly.

Adverse events which did not lead to serious injury or death, because a design feature protected against a malfunction becoming a hazard do not need to be reported. The protection against malfunction used needs to comply with relevant standards or documented design inputs for that type of device and take due account of technology and practice in existence. The risk has to be reduced to an acceptable level.

Examples of non-reportable adverse events:

*After a malfunction of an infusion pump it gives an appropriate alarm and stops (e.g. in compliance with relevant standards). There was no injury to the patient.

*Microprocessor-controlled radiant warmer malfunctions, reverts to an appropriate default condition and provides an audible appropriate alarm (e.g., in compliance with relevant standards). There was no injury to the patient.

¹ "malfunction" is synonymous with "fault".

* During radiation treatment, the automatic exposure control is engaged. Treatment stops. In accordance with the relevant standards the actual dose is displayed. Although patient receives less than optimal dose, patient is not exposed to excess radiation.

4.5 Negligible 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 negligible 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, it is reportable as an adverse event 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: Change in trend of these non-serious outcomes must be reported as specified in Appendix C.

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 negligible. No patients experienced adverse health effects.

* Particulates were found in a contact lens package. The likelihood of occurrence of serious injury is determined to be negligible. No patients experienced adverse health effects.

4.6 Expected and Foreseeable Side Effects.

Side effect: A secondary and usually adverse effect which is clearly identified in the manufacturer's labeling or is clinically well known² as being foreseeable and having a certain qualitative³ or quantitative predictability when the device was used and performed as intended.

Side effects do not need to be reported. It should also be noted that side effects are not associated with device malfunction, but rather they are associated with an adverse reaction by the patient to a device that is working properly.

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

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1. Some of these events are well known in the medical, scientific, or technology field; others may have been clearly identified during clinical investigation or clinical practice and labeled by the manufacturer.
 2. The conditions that lead to the side effect can be described but they are difficult to predict numerically – for example some patients will experience severe anxiety before they receive an injection

conclude in the face of events that they are foreseeable unless there is prior supporting information.

Examples of non-reportable adverse events

* A patient who is known to have claustrophobia experiences severe anxiety in the confined space of a MRI machine which subsequently led to the patient being injured.

* 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 product information.

* 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.

4.7 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 and if they have the same root cause for the products identified in that 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.

4.8 Reporting Exemptions Granted by a NCA.

Upon request by the manufacturer, and agreement by an NCA common and well-documented events may be:

- (a) Exempted from reporting or
- (b) changed to periodic or summary reporting..

5.0 Use Error

5.1 Reporting of Use Error

As with all reported device complaints, all potential use error events and potential abnormal use events should be evaluated by the manufacturer (see Appendix D for examples). The evaluation is governed by risk management, usability engineering, design validation, and corrective and preventive action processes. Results should be available, upon request, to regulatory authorities and conformity assessment bodies.

5.1.1 Use Error Resulting in Death or Serious Injury/ Serious Public Health Concern

Use error related to medical devices, which did result in death or serious injury or serious public health concern, should be reported by the manufacturer to the national competent authority.

5.1.2 Use Error not Resulting in Death or Serious Injury / Serious Public Health Concern

Use error related to medical devices, which did not result in death or serious injury or serious public health concern, need not be reported by the manufacturer to the national competent authority. Such events should be handled within the manufacturer's quality and risk management system, as described in Appendix D Section 6.0. A decision to not report must be justified and documented

5.1.3 Use Errors Becoming Reportable

Use errors become reportable by the manufacturer to the national competent authority when a manufacturer:

- notes a change in trend (usually an increase in frequency), or a change in pattern of an issue that can potentially lead to death or serious injury or public health concern.); or
- initiates corrective action to prevent death or serious injury or serious public health concern.

5.2 Consideration for handling abnormal use

Abnormal use need not be reported by the manufacturer to the national competent authority under adverse event reporting procedures. Abnormal use should be handled by the health care facility and appropriate regulatory authorities under specific appropriate schemes not covered by this document (see Appendix D:Annex B).

If manufacturers become aware of instances of abnormal use, they may bring this to the attention of other appropriate organizations and healthcare facility personnel.

6.0 To Whom to Report

Adverse Events must be reported to a National Competent Authority (NCA) according to applicable requirements in each jurisdiction.

7.0 Timing for Reporting

Upon becoming aware that an event has occurred and is associated with one of its devices, the medical device manufacturer must determine whether it is an adverse event. If reportable, the manufacturer must submit a report of the adverse event as soon as possible, but not later than 30-elapsd calendar days following the date of awareness of the event.

Adverse events that result in unanticipated death or unanticipated serious injury or represent a serious public health threat must be reported immediately by the manufacturer.

All other reportable events must be reported as soon as possible by the manufacturer, but not later than 30-elapsd calendar days following the date of awareness of the event.

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

All report times refer to when the NCA must first be notified. This notification may be in the form of an initial report, final report or trend report as defined in Appendix A Section B. The choice of report type depends on whether all the applicable data specified in Appendix A is available within the appropriate report time. If additional information is required, the manufacturer should provide a follow-up or final report as soon as the information is available or as requested by the NCA.

8.0 Universal Dataset for Adverse Event Reporting

Reports on Adverse events should include all available information in the Universal Dataset for Adverse Event Reporting provided in Appendix A.

Appendices

Appendix A: Universal Data Set for Manufacturer Adverse Event Reports

1.0 Introduction

This guidance represents a follow-up to the identification of the elements necessary for a minimum data set defined in SG2 N7. This new effort, identified as SG2 N32 expands the minimum elements, and represents all elements that should be included in any report from the manufacturer or authorized representative to the National Competent Authority (NCA).

2.0 Scope

This document identifies the various distinct and essential elements to be included in a reported adverse event. This document does not represent a format, which might be otherwise defined by the national authority to whom the report is sent.

3.0 References

This guidance is intended for the device manufacturer, or authorized representative, in accordance with the requirements of SG2 N7 and SG2 N21.

4.0 General considerations

1. **Dates** should be formatted as follows: 2 digit day, 3 letter month, 4 digit year, e.g., 01 JAN 2001
2. **Age**, and other timeframes, should specify if counted in days, months or years.
3. A **reasonable effort** should be made to address all elements defined below, however failure or inability to do so is not justification for failing to submit a report within the established timeframes.
4. **Electronic addresses** are desired whenever available.
5. Each field must be completed with the requested information or "NA" if not applicable to the event or "unknown" when the data is not available.
6. Please use the **comments** section at the end to provide any additional details that are relevant and not requested elsewhere.
7. In order to avoid the connotation of blame, information identifying the Health Care Facility or the User may be considered optional in certain NCA systems.
8. Manufacturers and NCAs need to be aware that patient privacy requirements must be honored where applicable.
9. NCAs may designate some elements to be eliminated or made optional.

5.0 Data Set Elements and Guidance

I. Administrative Information

- A. Report Control Number
 1. Mfr's Internal #
 2. # assigned by NCA to whom sent
 3. User Facility Report #

4. User Facility #

B. Report Type (select one)

1. Initial defined as the first information submitted by the manufacturer about a reportable event, but the information is incomplete and supplementary information will need to be submitted. This includes immediate notification
2. Follow-up defined as a report that provides supplemental information about a reportable event that was not previously available)
3. Final defined as the last report that the manufacturer expects to submit about the reportable event. A final report may also be the first report
4. Trend defined as information supplied as a result of trending in accordance with SG2 N36

C. Date of this report

D. Date the adverse event occurred

E. Classification of event: (ref N21, N33)

1. Unanticipated Death, unanticipated Serious Injury, or Serious Public Health Threat
2. All other reportable events

F. Mfr. awareness date defined as the date that a manufacturer first learned about a reportable event

G. Expected date of next report i.e., if this is not a "final" report, this represents the date when further information will be submitted to the NCA

H. Person, or authorized rep, submitting this report

1. Name of the contact person submitting the report
2. Company Name
3. Address
4. Phone
5. Fax
6. Electronic mail address

I. Identify to what other NCAs this report was *also* sent.

II. Clinical Event Information

- A. Event description narrative clarification: relevant information that might impact the understanding or evaluation of the adverse event AND that is not included elsewhere in this report. For example- "the

patient was confused prior to becoming trapped in the bed sides"; "the patient was a very low birth weight premature delivery and had a central line placed three days before onset of cardiac tamponade"; "the X-ray machine was over 20 years old and had been poorly maintained at the time of the adverse event", etc.)

- B. Number of patients¹ involved
- C. Number of devices involved

III. Healthcare Facility Information

- A. Name
- B. Address
- C. Phone
- D. Fax
- E. Electronic mail address
- F. Contact Name at the Site of the Event

IV. Device Information (Repeat this section for each device involved)

- A. Device Information
 - 1. Mfr. Name
 - 2. Contact Name
 - 3. Address
 - 3. Phone
 - 5. Fax
 - 6. Electronic mail address
- B. Operator of device at the time of the event (select from list below)
 - 1. Healthcare professional
 - 2. Patient
 - 3. Other Caregiver
 - 4. None defined as: problem noted prior to use
- C. Usage of Device (select from list below)
 - 1. Initial Use
 - 2. Reuse of Single Use Device
 - 3. Reuse of Reusable Device
 - 4. Re-serviced/Refurbished
 - 5. Other, (Please Specify)
- D. Generic Device Information
 - 1. Nomenclature System
 - 2. Nomenclature Code

3. Nomenclature Code Defined in Text
4. Brand Name
5. Model #
6. Catalogue #
7. Device identifiers e.g., serial #, batch #, software version #, etc.

E. Device Disposition/Current Location e.g., device has been destroyed, remains implanted in patient, was returned to the manufacturer, remains under investigation, etc.

F. Device approval information

1. Regulatory/National Competent Authority who approved device
2. Notified Body (NB) who approved device
3. Other 3rd party name who approved device
4. NB ID number
6. Document approval number

V. Results of Manufacturer's Investigation

A. Manufacturers Device Analysis Results Specify, for this event, details of investigation methods, results, and conclusions

B. Remedial Action/Corrective Action/Preventive Action

Specify if action was taken by manufacturer for the reported specific event or for all similar type products. Include what action was taken by the manufacturer to prevent recurrence. Clarify the timeframes for completion of various action plans.)

VI. Patient⁴ information (Repeat this section for each patient involved)

Provide individual patient information for each element as appropriate

- A. Age of patient at time of event - specify units of measure, i.e., days, months, or years
- B. Gender
- C. Weight in Kilograms (metric units will be assumed)
- D. List of Devices involved with each patient, see Section IV

⁴ Includes any affected individual eg user, patient, or third party.

E. Patient-focused Resolution of Events and Outcomes

1. Corrective action taken relevant to the care of the patient
2. Patient outcome

VII. Other Reporting Information (to be included in final reports only)

Is the mfr aware of similar events with this device with the same root cause?

Y/N

If yes, provide the number of the events - The " number" should be specified in terms of event per unit sold, or the number of event per unit sold / in use in a region, etc.

Providing this information is considered to be a burden to industry and NCA's should consider carefully in making this a national requirement (see item 9 under General Considerations).

VIII. Comments

IX. Manufacturer Disclaimer

Appendix B: Timing of Adverse Event Reports

1.0 Introduction

It is acknowledged in the issuance of this guidance that various national jurisdictions have current adverse event report timing requirements that differ from the recommendations contained herein. Consequently, establishment of harmonized reporting times has been controversial within Study Group 2 and the wording in this document represents the most reasonable compromise that has been produced to date. Due to differences in laws and regulations in different regions it may not be possible to harmonize all these current differences without changes that are beyond the authority of the National Competent Authorities to implement administratively. However, it is the view of GHTF Study Group 2 that issuing this guidance will nevertheless serve as a useful model in the development of adverse event reporting requirements in national jurisdictions that currently do not have a reporting system. This guidance is also considered a model for future change of existing reporting systems as they continue to evolve.

An examination of adverse event report timing requirements in Europe, USA, Canada, Australia, and Japan reveals a diversity of requirements ranging from 2 days to 30 days depending on the nature of the reportable event.

Study Group 2 has examined data provided by member manufacturers to determine the amount of time involved to conduct an investigation of adverse events for different types of devices. There was a wide spread in the distribution of investigation times. The median investigation time required for diagnostic imaging devices was approximately two weeks (15 days) and even longer for several other types of devices. More than 50 % of device events required more than two weeks to complete an investigation of the event. Thus, it is concluded that reporting of adverse events within the first two weeks is likely to be based on an incomplete investigation and may require a subsequent follow-up report as well.

This conclusion is consistent with the experience at FDA where reporting requirements have been in effect the longest. FDA has received a large number of follow-up reports and subsequently changed the reporting timing from 5 days (death & serious injury) and 15 days (malfunction) to 30 days for most reports. While it is desirable that adverse event reports be timely, it is also desirable that the information be accurate.

2.0 Scope

The Global Harmonization Task Force (GHTF) Study Group 2 (SG2) has developed a regulatory guidance document for manufacturers regarding adverse event reporting. This guidance is referenced as SG2 N21R8. It includes guidance for the regulatory authorities about reporting of adverse events that result in death or serious injury or certain types of near incidents. It does not stipulate timeframes for submitting adverse event reports. It is therefore proposed that a statement of reporting timing is included in SG2 N21R8 and it include the wording recommended in this guidance.

3.0 References

Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative, GHTF SG2 N21R8

4.0 Definitions

Immediately:

For purposes of adverse event reporting, immediately means as soon as possible, but not later than 10 elapsed calendar days following the date of awareness of the event.

Serious public health threat:

Any event type, which results in imminent risk of death, serious injury, or serious illness that may require prompt remedial action.

Unanticipated:

A death or serious injury is considered unanticipated if the condition leading to the event was not considered in a risk analysis performed during the design and development phase of the device. There must be documented evidence in the design file that such analysis was used to reduce the risk to an acceptable level.

5.0 Report Times

Upon becoming aware that an event has occurred and is associated with one of its devices, the medical device manufacturer must determine whether it is an adverse event.

Adverse events that result in unanticipated death or unanticipated serious injury or represent a serious public health threat must be reported immediately by the manufacturer.

All other reportable events must be reported as soon as possible by the manufacturer, but not later than 30-elapsed calendar days following the date of awareness of the event.

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

All report times refer to when the NCA must first be notified. This notification may be in the form of an initial report, final report or trend report as defined in GHTF N32, "Manufacturer Universal Data Set". The choice of report type depends on whether all the applicable data specified in N32 is available within the appropriate report time. If additional information is required, the manufacturer should provide a follow-up or final report as soon as the information is available or as requested by the NCA.

Appendix C: Trend

1.0 Introduction

The GHTF document “Adverse Event Reporting Guidance for the Medical Device Manufacturer or its Authorized Representative” (GHTF SG2 N21 R8) specifies principles for reporting of adverse events by manufacturers. It also includes provisions about common and well-documented events that may be exempt by National Competent Authorities (NCAs) from reporting or changed to periodic reporting upon request by the manufacturer and agreement from the NCA.

The present document describes the criteria for identifying a significant increase in the rate of adverse events and hence for submission of a trend report to the NCA, irrespective of whether such events are individually reportable, periodically reportable or currently exempt from reporting as agreed to by the NCA.

It is also important to recognize that there are circumstances when a manufacturer should take action immediately without waiting for a trend to occur. It may be based on the severity of the event, or by perceived risks associated with the adverse event(s) regardless of the number of events.

This document is not intended to define statistical techniques for trending or to place additional requirements beyond the trending of complaints, which forms an integral part of a manufacturer’s quality system. Instead, it explains the reasons for the importance of adverse event trending and reporting and also provides some guidance on key aspects.

2.0 Definitions

For the purpose of this document, “manufacturer” is limited to the organization that establishes and maintains the QMS associated with the product, it does not include distributors of medical devices.

3.0 Trend Reporting for Adverse Events

A trend report should be made where there has been a significant increase in the rate of:

3.1 Already reportable events

A significant increase in the rate of reportable events presents a manufacturer with a new piece of information about his device or its performance in a clinical setting. Unless there is a corresponding trend in the product market as a whole, it is less likely that the NCA will be able to detect this change as only the manufacturer with complete access to his market data can create a reasonable facsimile of rates and can estimate trends.

3.2 Adverse events that are currently exempt from reporting

An exemption from reporting certain reportable events is usually provided on the basis that the NCA believes the event is well characterized and they and the industry have done as much as is justified at that time to prevent further adverse events. However, a significant increase (see explanation below) in the rate of these exempt events may indicate an

underlying change in the performance of the manufacturer's product or in its use by clinicians, patients or other customers. Either situation would be of considerable value for the NCA and is an appropriate reason for submission of a report to the NCA as soon as the manufacturer becomes aware of the change in rate.

3.3 Adverse events scheduled for periodic reporting

The rationale for reporting a change in the rate of events for periodic reporting follows from the arguments above. Firstly, periodic reports of numerator (adverse event) data without denominators (devices on the market or in use) do not provide the NCA with the ability to estimate trends appropriately. Secondly, although periodically reported events may enable the NCA to examine general market trends, the individual manufacturer is responsible for indicating potentially important changes in product safety.

4 Adverse Event Trending

The decision to file a trend report should be based on the occurrence of a significant increase in the number of adverse events.

4.1 Trending procedure and significant increase

Based on the diversity of the medical devices in the market it is not meaningful to define a single trending procedure valid for all devices. Depending on the type of device (e.g. IVD, implant, diagnostic and therapeutic device, surgical and dental instrument, hearing aid, compression, etc.), the devices risk classification, the number of products delivered, single or multiple use of devices, devices with traceability requirements, unavailable information on device disposals and other parameters a manufacturer must adopt a trending procedure which is applicable and adequate for his operations and devices. Basic methods for performing trending can be found in the literature (e.g. for statistical quality control) and will not be repeated in this document.

While for many manufacturers the use of simple graphs and charts will be sufficient, the implementation of more sophisticated methods will be advisable for others. It is important that valid statistical methods are used for trend evaluation. NCAs may request the manufacturer to demonstrate that the applied method is appropriate for the particular case.

It is less easy, however, to find in the medical device area a definition in the literature of what constitutes a significant increase in the rate of adverse events. The discussion below explains "significant increase" in statistical trending. Concurrently, this document provides guidance to manufacturers on how a creditable baseline for trending can be established and provides information to NCAs that might facilitate decisions regarding reporting exemptions for devices with well-established baselines.

4.2 Complaint trending and adverse event trending

Complaint trending as an established quality system requirement provides the basis on which manufacturers are asked to accumulate and analyse their data. Since complaints come from the data source from which reportable adverse incidents are identified, trending of adverse events uses essentially the same methods as trending of complaints. For both trending processes the database, in the form of the complaint file, is the same.

The difference:

- Trending of complaints may lead to the discovery of a complaint trend (and the appropriate corrective and preventive action) but not necessarily to a report to the NCA.
- Trending of adverse events may lead to a report to the NCA.

To summarise: the method for the trend evaluation of both complaints and adverse events can be the same while the decision making process and following activities are different.

5 Statistical Trending Example and Significant Increase

5.1 Basic trending parameters

The raw data to be gathered for trending are the number of events (n) in a given time interval (t) and the related used product volume (by clinicians, patients) in the market (d) during that time interval. One data-point (i) = n/d is calculated for each time interval, and for the purposes of this document is defined as the observed incidence expressed as a percentage. Patient exposure over time will need to be measured or estimated for the denominator (d), in place of the used product volume, for devices such as medical implants that are continually in use. However, where data about exposure to use are not known to a manufacturer, the number of products in the field may have to be used as the denominator (d).

If relevant, (e.g., for implants) trending might also be initiated for clinical findings or other variables such as age, weight and gender of patients, age of the device) and others.

The Baseline (I_B) and Threshold (I_T) against which the observed incidence is compared for establishing the trend are also expressed as percentages of the related used product volume in the market or exposure to use. If the used volume for a related manufacturer's product is too low for a meaningful statistical measure, each single adverse event should be reported to the NCA. The quality of the statistics increases with both the number of events and the installed volume in the market. Care should be taken when identifying the data to be used for trending. Only market areas where adverse event reporting is established should be included in the trending. Otherwise the frequency of known events may not match the used volume, leading to wrong results.

5.2 Baseline I_B

For establishing a realistic (e.g. to avoid under-reporting) baseline to start with, multiple tools and methods can be used such as risk analysis, analysis techniques for dependability and reliability testing (see also respective IEC standards and application guides) etc. Another important source of information is historical data from the manufacturer's or his competitor's equivalent devices. Further information can also be found in medical and scientific publications.

If there is insufficient information for the determination of a credible and statistically proven baseline, individual adverse events should be reported.

5.3 Threshold (I_T) and Time Interval (t)

The typical number of events in a given time interval, e.g. one month, varies depending upon the product type and may range from 1 or 2 events up to a few hundred.

The time interval should be long enough to gather sufficient data for the analysis depending upon the volume of products sold and adverse events reported. For higher volume products a typical time interval is 1 month. It is important that the time interval is short enough to facilitate timely corrective action, especially in case of high-risk products.

The upper value of the normal range of variation that specifies the trending, Threshold I_T , will be different depending on the product category.

5.4 A significant increase in observed incidence

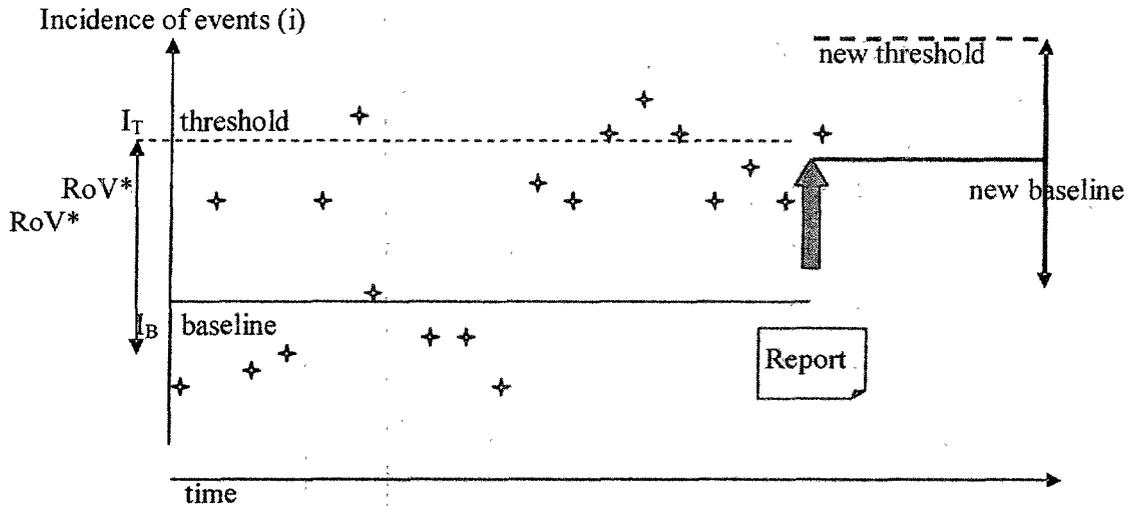
A sustained increase of the observed incidence (i) above the baseline over a certain number of time intervals will constitute a significant increase, and should trigger a trend report to the NCA (see figure 1). Whether or not the increase is considered to be sustained is tested and determined by the chosen statistical methodology. The trend report should be filed as soon as the significant increase is identified.

Depending on the product volume in the market, a “significant increase” might be identified as a result of any of the following:

- (a) a rapid and continuous increase in (i) over a limited number of time intervals for high volume products (eg over 1 - 3 months)
- (b) a slow and continuous increase in (i) over a larger number of time intervals for low volume products (eg over 3 - 6 months),

Although an upward shift in the baseline will follow identification of a significant increase, as a basic quality system requirement, corrective and preventive actions needs to be initiated to evaluate and eliminate the root cause of the problem in order to reverse the upward trend of the baseline and return it to the previous level or lower.

Figure 1: Upward Shift of baseline and trend report filing



* normal Range of Variance

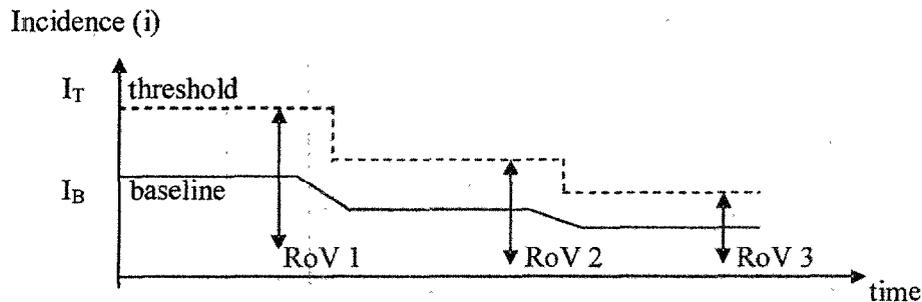
Note: Only one datapoint per time interval

5.5 Baseline Improvements

If there is a sustained decrease in incidence over successive time intervals this will lead to a reduction in the baseline and threshold which should then be used for future trending. (see Figure 2).

Such downward shifts in the baseline, which can relate to product/process improvements, or refinement of clinical indications/usage - are positive developments leading to reduced numbers of adverse events and, to cost savings on the manufacturer's side and to the overall healthcare system.

Figure 2: Baseline improvements



5.6 Exceptional cases

If there are sudden large increases in the incidence (i) or number of events (n), whether or not they are sustained, it is recommended to file a report with the NCA even if the trend evaluation does not trigger a report or the time interval for the actual trending period has not finished. A report should be filed as soon as the exceptionally high value is identified and an associated corrective action initiated even before the trend is confirmed.

Appendix D: Use error

1.0 Introduction

The Global Harmonization Task Force (GHTF) Study Group 2 (SG2) developed a regulatory guidance document for manufacturers regarding adverse event reporting. This guidance is referenced as SG2 N21R8¹. N21 includes guidance about reporting of adverse events that result in death or serious injury or certain types of near incidents. N21 also includes the consideration that certain types of failures may be exempt from reporting under regulatory vigilance procedures, but does not include a specific proposal on reporting of use errors. This document (N31) gives a proposal for reporting of use errors with medical devices by their manufacturer or authorized representative.

There is increased international focus on errors in the use of medical devices, and this document (N31) divides the broad category into two defined and distinct groups: use error and abnormal use. Both groups must be evaluated within the manufacturer's quality system and the results documented but only the use error group can be controlled by the manufacturer's quality system corrective and preventive action requirements, design validation, usability engineering, and risk management processes. By its nature the use error group usually involves a degree of uncertainty as to the root cause, but the risks can be managed by the manufacturer in conjunction with the national regulator and conformity assessment body. The risks involved with abnormal use must be managed between the healthcare facilities, national regulator or other responsible organization.

2.0 Scope

This document represents a global model, which provides guidance on the type of adverse events involving use errors, that should be reported by manufacturers or their authorized representatives to regulatory authorities.

The reporting of adverse events by the operator or user of medical devices is outside the scope of this document (N31), although some consideration for a user reporting scheme is given in Annex B.

3.0 Definitions

3.1 Use error:

Act, or omission of an act, that has a different result to that intended by the manufacturer or expected by the operator.

Note Use error includes slips, lapses, mistakes and reasonably foreseeable misuse.

Definition taken from AAMI HE 74:2001² and IEC/CD2 60601-1-6:2002³. See also Annex A for examples of potential use errors.

3.2 Abnormal use:

Act or omission of an act by the operator or user of a medical device as a result of conduct that is beyond any reasonable means of risk control by the manufacturer.

Note Foreseeable misuse that is warned against in the instructions for use is considered abnormal use if all other reasonable means of risk control have been exhausted.

Definition taken from IEC/CD2 60601-1-6:2002³. See also Annex A for examples of potential abnormal use.

3.3 Operator:

Person handling equipment.

Definition taken from IEC 60601-1, 2nd Ed.⁴

3.4 User:

Authority responsible for the use and maintenance of equipment.

Definition taken from IEC 60601-1, 2nd Ed.⁴ GHTF-SG2 acknowledges that the term “user” might designate different persons under various regulatory systems.

4.0 Proposal for reporting of use errors

As with all reported device complaints, all potential use error events, (examples are given in Annex A), and potential abnormal use events dealt with in paragraph 5.0, should be evaluated by the manufacturer. The evaluation is governed by risk management, usability engineering, design validation, and corrective and preventive action processes. Results should be available, upon request, to regulatory authorities and conformity assessment bodies.

4.1. Use error resulting in death or serious injury/ serious public health concern

Use error related to medical devices, which did result in death or serious injury or serious public health concern, should be reported by the manufacturer to the national competent authority.

4.2. Use error not resulting in death or serious injury / serious public health concern

Use error related to medical devices, which did not result in death or serious injury or serious public health concern, need not be reported by the manufacturer to the national competent authority. Such events should be handled within the manufacturer’s quality and risk management system, as described in 6.0 below. A decision to not report must be justified and documented (see SG2 N21¹).

4.3. Use errors becoming reportable

Use errors become reportable by the manufacturer to the national competent authority when a manufacturer:

- notes a change in trend (usually an increase in frequency), or a change in pattern (see SG2 N36⁵) of an issue that can potentially lead to death or serious injury or public health concern.); or
- initiates corrective action to prevent death or serious injury or serious public health concern.

5.0 Consideration for handling abnormal use

Abnormal use need not be reported by the manufacturer to the national competent authority under adverse event reporting procedures. Abnormal use should be handled by the health care facility and appropriate regulatory authorities under specific appropriate schemes not covered

by this document (see Annex B).

If manufacturers become aware of instances of abnormal use, they may bring this to the attention of other appropriate organizations and healthcare facility personnel.

6.0 How to reduce errors associated with medical devices

Errors associated with the use of medical devices have been reported in studies^{6,7}, in the range of 60-70%, as the cause of accidents with medical devices. Such errors have historically been called “user error”, “operator error”, and “human error”. IEC 60601-1⁴ Electrical medical equipment identifies human error as a hazard with medical devices, but remains silent under clause 46 in the 1988 edition, stating “under development”.

Globally harmonized medical device regulation requires that medical devices be designed and manufactured in such a way that they will not compromise the clinical condition or the safety of the patient, or the safety and health of operators or other persons. In addition, risks must constitute acceptable risks when weighed against the benefits to the patient. This essential principle is being accepted globally. (SG1 N20R5: Essential principles of safety and performance of medical devices⁸ and ISO 16142: Guide to the selection of standards in support of recognized essential principles⁹).

The risk reduction approach has resulted in European and International standards on risk analysis EN 1441¹⁰ and ISO 14971-1¹¹. The scope has been enlarged to cover risk management over the life cycle of the device. ISO 14971, Risk management¹² was formally accepted as an international standard in the year 2000. It requires that risk is analyzed and reduced to an acceptable level for the intended use or intended purpose, and also for the reasonably foreseeable misuse of a medical device. Consequently, errors relating to the use of medical devices have been designated “use errors” to avoid the connotation of blame on the operator or user or on the device and to differentiate them from abnormal use defined below. The term “use error” is defined in the IEC/CD2 60601-1-6³ as an act which has a different result than intended by the manufacturer or different result than expected by the operator. Examples of potential use errors are given in Annex A.

A process standard, IEC 60601-1-6: Usability³, is being developed describing the usability engineering process, and provides guidance on how to implement and execute the process. This guidance was developed by the Association for the Advancement of Medical Instrumentation (AAMI) and published as HE 74:2001². AAMI also plans to revise AAMI HE 48:1993¹³ which provides ergonomic data compilation. Guidance on operator and user training information to be provided by the manufacturer is also being developed.

IEC 60601-1-6, Usability³, excludes abnormal use from its scope. Abnormal use is an act or an omission of an act by the user or the operator as result of conduct that is beyond any reasonable means of risk control by the manufacturer of the medical device. Examples of potential abnormal use are given in Annex A

ISO TC210 is revising ISO 13485: Quality System for Medical Devices¹⁴, (EN 46001¹⁵ equivalent), in line with the revision of ISO 9001:2000¹⁶. The revision of the quality system standard is scheduled for the year 2003. ISO 9001 contains elements of customer satisfaction in complaints or corrective action requirements. ISO TC210 will also revise ISO

14969:Guidance for quality systems¹⁷, and enlarge on the feedback of use errors. This will be incorporated into several variables: into design considerations through the corrective and preventive action process, into design validation by using usability engineering, and into risk reduction and risk management processes over the life cycle of the medical device.

As discussed above, there is increased focus on use errors, and they have to be separated from abnormal use. This is being incorporated into quality system corrective and preventive action requirements, usability engineering, design validation, and risk management processes. For example, use errors will be evaluated by the manufacturers and documented, in places like design dossiers, and will be accessible to regulatory authorities and conformity assessment bodies.

7.0 References

1. GHTF -SG2 N21R8, *Adverse event reporting guidance for the medical device manufacturer or its authorized representative*, June 30, 1999
2. AAMI HE 74:2001, *Human factor design process for medical devices*.
3. IEC/CD2 60601-1-6:2002, *Medical electrical equipment – Part 1: General requirement for safety – Collateral standard: 6, Usability*.
4. IEC 60601-1:1988, *Medical electrical equipment – Part 1-6: General requirements for safety*
5. GHTF-SG2 N36, *Manufacturer trend reporting of adverse events*, June 30, 2000
6. J. Cooper, R.Newbower, R. Kitz, *An analysis of major errors and equipment failures in anesthesia management: consideration for prevention and detection: anesthesiology*, 60:34-42,1984
7. S.Bleyer, *Medizinische technische Zwischenfälle in Krankenhäusern und ihre Verhinderung*, in: Anna W, Hartung C (Hrsg.) *Mitteilungen des Instituts für Biomedizinische Technik und Krankenhaustechnik der Medizinischen Hochschule Hannover*, 1992.
8. SG1 N20R5, *Essential principles of safety and performance of medical devices*
9. ISO/TR 16142:1999-12, *Medical devices – Guidance on the selection of standards in support of recognized essential principles of safety and performance of medical devices. Guide to the selection of standards in support of recognized essential principles*.
10. EN1441:1997-10, *Medical devices - Risk analysis* (Document being replaced by EN ISO 14971:2000-12 with three year transition to 2003-12)
11. ISO 14971-1:1988-10, *Medical devices - Risk management – Part 1: Application of risk analysis* (Document being replaced by ISO 14971:2000-12 with three year transition to 2003-12)
12. ISO 14971:2000-12, *Medical devices – Application of risk management to medical devices*
13. AAMI HE48:1993 *Human factors engineering guidelines and preferred practices for the design of medical devices*
14. ISO 13485:1996-12, *Quality systems – Medical devices – Particular requirements for the application of ISO 9001*.
15. EN 46001:1996-08, *Quality systems - Particular requirements for the application of EN ISO 9001*
16. ISO 9001:2000-12, *Quality management systems – Requirements*

17. ISO 14969:1999-06, *Quality systems – Medical devices – Guidance on the application of ISO 13485 and ISO 13488*

ANNEX A

EXAMPLES OF USE ERROR AND ABNORMAL USE

1. Potential use errors:

Complaint reports received of events occurring despite proper instructions and proper design according to manufacturer's analysis.

- Operator presses the wrong button.
- Operator misinterprets the icon and selects the wrong function.
- Operator enters incorrect sequence and fails to initiate infusion.
- Operator fails to detect a dangerous increase in heart rate because the alarm limit is set too high and operator is over-reliant on alarm system.
- Operator cracks catheter connector when tightening.
- A centrifugal pump is made from material that is known to be incompatible with alcohol according to the labeling, marking, and product warnings provided with the pump. Some pumps are found to have cracked due to inadvertent cleaning with alcohol.
- Unintentional use of pipette out of calibration range.
- Analyzer placed in direct sunlight causing higher reaction temperature than specified.
- MRI system and suite have large orange warning labels concerning bringing metal near the magnet. Technician brings an oxygen tank into presence of magnet and it moves swiftly across the room into the magnet.

2. Potential abnormal uses:

Complaint reports received of events occurring despite proper instructions, and proper design, and proper training according to manufacturer's analysis determined to be beyond any reasonable means of the manufacturer's risk control.

- Use of a directly medical device in installation prior to completing all initial performance checks as specified by the manufacturer.
- Failure to conduct device checks prior to each use as defined by the manufacturer.
- Continued use of a medical device beyond the manufacturer defined planned maintenance interval as a result of operator's or user's failure to arrange for maintenance.
- Contrary to the instructions for use, the device was not sterilized prior to implantation.
- Pacemaker showed no output after use of electrocautery device on the patient despite appropriate warnings.
- Product analysis showed that the device was working in accordance to specifications, further investigation revealed that the operator was inadequately trained due to failure to obtain proper training.
- During placement of a pacemaker lead, an inexperienced physician or other non-qualified individual perforates the heart.
- The labeling for a centrifugal pump clearly indicates that it is intended for use in bypass operations of less than 6 hours in duration. After considering the pump options, a clinician decides that the pump will be used in pediatric extra-corporeal membrane oxygenation (ECMO) procedures, most of which may last several days. A pump fails

due to fatigue cracking and patient bled to death.

- Safety interlock on a medical laser removed by operator or user.
- Filter removed and intentionally not replaced resulting in particulate contamination and subsequent device failure.
- Tanks delivered to a health care facility are supposed to contain oxygen but have nitrogen in them with nitrogen fittings. The maintenance person at the health care facility is instructed to make them fit the oxygen receptacles. Nitrogen is delivered by mistake resulting in several serious injuries.
- Use of an automated analyzer regardless of the warnings on the screen that calibration is to be verified.
- Pacemaker patient placed into MRI system with the knowledge of the physician.
- Ventilator alarm is disabled, preventing detection of risk condition.
- Patient's relative intentionally altered infusion pump to deliver a lethal overdose of the infusing drug to the patient.
- Home care worker uses bed rails and mattress to suffocate patient.

ANNEX B

Considerations for Adverse Event Reporting by the Operator or User of Medical Devices (User Reporting)

Abnormal use, i.e. act or omission of an act by the operator or user of a medical device that is a result of conduct that is beyond any reasonable means of risk control by the manufacturer should be reported by the operator or user to the health care facility, following internal procedures based on anonymity and non-punitive, for evaluation, feedback to the reporting person or facility and eventual corrective actions by the health care facility, in consultation with the manufacturer, if necessary, i.e., where a medical device may be involved.

If national authorities regulate the user reporting, it should follow the principle of anonymity and non-punitive, evaluation, feedback to the reporting person or facility and eventual corrective action. In cases where a medical device is involved, the manufacturer should be informed about the adverse event by the Competent Authority upon receipt of such reports from the user.