WATSON Laboratories, Inc.
A Subsidiary of Watson Pharmaceuticals, Inc

2183 '03 APR 25 A9:00

24 April, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

**RE: Docket 02N-0528; Risk Management, Public Workshop**

With this letter, Watson Laboratories is submitting comments on FDA's recently published concept papers on risk management. Our comments are included in the enclosed 3-page document. We have also included as supplemental material a copy of draft standard AAMI/ISO/IEC 14971, 3rd edition: *Medical devices – Risk management – Application of risk management to medical devices.*

If you have any questions about our comments or the supplemental material, please call me direct at (801) 588-6377, or I may be reached via e-mail at john.smith@watsonpharm.com.

Best Regards,

John W. Smith
Associate Director, Regulatory Affairs

02N-0528 C 3

Research Park, 417 Wakara Way, Salt Lake City, UT 84108 • Tel: 801/588-6200 • Fax: 801/588-6212

Watson applauds FDA's attempt to establish uniform expectations for risk management. Watson also applauds FDA's inclusion of the public in its process for developing guidance in this area. While a formal approach to risk management is appropriate, and represents a major step forward in drug development, we feel FDA's proposed approach needs improvement in a few key areas.

First, FDA's proposed processes for risk management are all placed too late in the development process. The concept papers discuss late-stage trials, labeling and post-approval activities. While these tools are valid, and should be included in a complete risk management process, they are not the entire process. Emphasizing these late-stage tools misses earlier-stage opportunities to address potential risks. We believe that a more balanced approach, including both early and late stage tools, is more appropriate.

Standard risk management techniques for other products include early and iterative assessment through analytic processes, like Failure Mode and Effects Analysis (FMEA) or Fault Tree Analysis (FTA). These tools are prospective rather than retrospective, and are widely accepted as effective risk assessment methods. These kinds of analytic techniques could easily be extended to drugs, using early development information (e.g., animal toxicity studies, pharmacology information, computer simulation, etc.). This valuable early information should inform later discussions with FDA about risk analysis and management, rather than waiting until late in the process to agree on a risk management strategy. Good design practices, widely accepted in many industries, recognize that analyzing and addressing risks early in the design process is more efficient and cost-effective than doing it late in the process.

Second, FDA's proposed approach attempts to force all drugs into the same model. Each drug is different, with its own risks and benefits. Risk management should take into account each drug's unique characteristics; a one-size-fits-all process is impossible and inappropriate. We agree with FDA's statements in the public workshop of April 9 – 11, 2003 that each risk management program should be evaluated on a case-by-case basis. Following that logic, we recommend that the specific list of studies that all drugs should *perform* (contained in lines 340 to 345 of FDA's concept paper on premarketing risk assessment) be revised to be a list of studies that all drugs should *consider*. If scientific information about a drug suggests that QT prolongation could be an issue, then it should be tested. But large numbers of drugs would not require this testing (e.g., many dermatological drugs) and should not be required to perform it.

Third, FDA focuses too much on nomenclature and classification, and not enough on process. FDA's attempt to draw a bright line between which drugs require a formal risk management program and which do not is inappropriate and misleading. All drugs require a risk management program of some kind; the depth and breadth of the activities should be commensurate with the individual drug's risks and benefits. Creating arbitrary levels and classifications for discrete types of risk management programs is inappropriate and distracting. Drug developers and FDA will inevitably spend too much time arguing over which level a product should be in, rather than focusing on what risk management activities are most appropriate. Additionally, attempting to define the difference between a risk management plan and a risk management program is too fine a focus on details. All

activities, plans, programs, studies, processes and so on fall under the general rubric of Risk Management.

Fourth, FDA's risk management scheme relies far too much on labeling (i.e., package and patient inserts). While this is understandable, given FDA's regulatory framework, manufacturers have few incentives to keep their labeling up to date. The regulatory obstacles to making frequent labeling changes ensure that drug labeling will usually not reflect the most current and complete information about a drug.

Beyond the issue of keeping labeling current, however, this scheme has a more fundamental flaw. Standard engineering practices for risk management have a three-tiered approach to addressing risks. In preferred order, those approaches are:

1. Addressing risks through design

2. Providing alarms or guards against the risk

3. Providing warnings and instructions.

Of the three, warnings and instructions are widely acknowledged to be the least effective risk management technique. Yet, FDA's approach relies on these controls exclusively.

To provide some examples of how FDA's proposed risk management process could be improved, we have enclosed with these comments a copy of a draft international standard: AAMI/ISO/IEC 14971, 3rd edition: *Medical devices – Risk management – Application of risk management to medical devices*. This standard is a voluntary consensus standard, written and maintained by device regulators and manufacturers; it represents the best thinking of the international medical device community. This standard has already been through several cycles of improvement over many years. FDA's own Center for Devices and Radiological Health (CDRH) has recognized the validity of the current edition of this standard, and will accept conformity to the standard as evidence of a satisfactory risk management process[1].

While we are not suggesting that CDER adopt a totally self-certified risk management process for drugs, we do suggest that this document provides rich and valuable information on how a risk management process should be structured. The standard lays out several stages for the risk management process, and clearly states that the process is an iterative one[2]:

> The manufacturer shall establish and maintain a process for identifying hazards associated with a medical device, estimating and evaluating the associated risks, and controlling these risks, and

---

[1] See the CDRH web page:
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/Detail.CFM?STANDARD__IDENTIFICATION_NO=5188

[2] Page 4, line 216 of the draft standard

monitoring the effectiveness of the controls throughout the life cycle. This process shall be documented and shall include the following elements:

- risk analysis;
- risk evaluation;
- risk control; and
- post-production information.

The flowchart on page 5 of the draft standard is particularly useful for illustrating a risk management process. Beginning with section 4 of the draft standard[3], the elements of a good risk management process are laid out. Rather than repeat them here, we urge CDER to read these sections. We also urge CDER to read the Annexes to the draft standard; they supply information supporting the standard's development and further illustration of the various engineering techniques available for risk identification and estimation.

In particular, Annex G contains a sample list of questions that manufacturers can use to identify hazards. While this list of questions obviously applies more to devices than drugs, we believe a similar list of questions could be used to identify hazards associated with a specific drug. We suggest that, rather than a specific list of studies that all drugs should perform (see lines 340 to 345 of FDA's concept paper on premarketing risk assessment), a sample list of questions similar to ISO 14971's Annex G could be used to make better-informed decisions about what potential hazards should or should not be evaluated.

Not all of our comments are negative. We believe FDA's proposal to maintain a list of "best practices" for risk management on the FDA web site is a very good idea. This list could be maintained and updated far more frequently than published guidances. Since the practice of Risk Management for drugs is bound to evolve rapidly over its first few years, keeping a centralized list of examples constantly updated is the best way to spread information.

In conclusion, Watson believes FDA has made a good start on developing a Risk Management framework. However, the process needs to better balance the needs for late-stage controls with sound development and design practices. Putting all the controls at the end of the design process is too expensive and inefficient.

---

[3] Page 7, line 290 of the draft standard

**AAMI Order Code: 14971-D**

**DOCUMENT: Future AAMI/ISO/IEC 14971 3ed., 19-Mar-03 Committee Draft for Vote**

***Medical devices - Risk management - Application of risk management to medical devices***

Public Review Draft Designation: AAMI/DS-1 14971

AAMI has circulated this draft to committee members for comment and vote. Consensus on this draft will be developed by AAMI/QM/WG 04, Application of risk management to medical devices. Interested parties may submit public review comments, in writing, to:

AAMI
1110 N. Glebe Road
Ste 220
Arlington, VA 22201-4795
ATTN: Hillary Woehrle
Fax: 703-276-0793; Email: hwoehrle@aami.org

This is a proposed US adoption of a draft ISO document (ISO/CD-V).

**COMMENT DEADLINE: 13 June 2003**

Comments should be received by AAMI by the above deadline (earlier if possible) to ensure their consideration by the Committee.

**INSTRUCTIONS FOR COMMENTING:**

Comments should be set forth as follows:

a. Section number, section heading, and page number of document;
b. Comments/objection;
c. Rationale for comment/objection; and,
d. Suggested alternative text to resolve comment/objection.

NOTE–The above format is not required for comments concerning typographical errors; simply identify the nature and location of the error (eg, by page, paragraph, and line number).

Failure to comply fully with these instructions may cause comments to be considered non-persuasive.

An electronic Public Reviewer form is available from the AAMI website at:

WORD97 http://www.aami.org/standards/downloadables/aamirevf.doc

Acrobat (pdf) http://www.aami.org/standards/downloadables/aamirevf.pdf

**Please be sure to identify the document by designation: 'AAMI/DS-1 14971, Medical devices - Risk management - Application of risk management to medical devices,' and include your name, address, phone number, fax number and email address in the event we need to contact you about your comments.**

**AAMI/CDV-1 14971**
(AAMI/DS-1 14971)
2003-03-19
(Revision of ANSI/AAMI/ISO 14971:2000)

**Committee Draft for Vote**
(Proposed Draft)

AAMI/ American National Standard

**NOTE** - This document is still under study and subject to change. It should not be used for reference purposes.

# Medical devices - Risk management - Application of risk management to medical devices

**Abstract:** Specifies a procedure for the manufacturer to identify the hazards associated with medical devices and their accessories including in vitro diagnostic devices, estimate and evaluate the risks, control these risks, and monitor the effectiveness of the control. This standard does not specify acceptable risk.

**Keywords:** risk management, hazard

**Association for the Advancement of Medical Instrumentation**
1110 N. Glebe Road, Suite 220, Arlington VA 22201-4795
Phone 703/525-4890 Fax 703/276-0793 Internet www.aami.org

## AAMI Standard

This Association for the Advancement of Medical Instrumentation (AAMI) standard implies a consensus of those substantially concerned with its scope and provisions. The existence of an AAMI standard does not in any respect preclude anyone, whether they have approved the standard or not, from manufacturing, marketing, purchasing, or using products, processes, or procedures not conforming to the standard. AAMI standards are subject to periodic review, and users are cautioned to obtain the latest editions.

CAUTION NOTICE: This AAMI standard may be revised or withdrawn at any time. AAMI procedures require that action be taken to reaffirm, revise, or withdraw this standard no later than 5 years from the date of publication. Interested parties may obtain current information on all AAMI standards by calling or writing AAMI.

*Published by*

Association for the Advancement of Medical Instrumentation
1110 N. Glebe Road, Suite 220
Arlington, VA 22201-4795



Printed in the United States of America

| COMMITTEE DRAFT ISO/CD 14971 | |
|---|---|
| Date<br>2003-03-19 | Reference number<br>ISO/TC 210 / SC **N 215** |
| Supersedes document<br>ISO/TC 210 N185 | |

**WARNING:** This document is not an International Standard. It is distributed for review and comment. It is subject to change without notice and may not be referred to as an International Standard.

**ISO/TC 210 / SC**

Title

Quality management and corresponding general aspects for medical devices

Secretariat AAMI (for ANSI)

Circulated to P- and O-members, and to technical committees and organizations in liaison for:

☐ discussion at on
[venue/date of meeting]

☒ comments by
[date]

☒ approval for registration as a DIS in accordance with 2.5.6 of part 1 of the ISO/IEC Directives, by

[date]

(P-members vote only: ballot form attached)

**P-members of the technical committee or subcommittee concerned have an obligation to vote.**

*English title*

**Medical devices - Application of risk management to medical devices (Revision of ISO 14971:2000)**

*French title*

**Dispositifs médicaux — Application de la gestion des risques aux dispositifs médicaux**

*Reference language version:* ☒ English ☐ French ☐ Russian

Introductory note

This Committee Draft (CD) of the 2nd edition of ISO 14971 was prepared by the ISO/TC 210-IEC/SC 62A Joint Working Group 1, *Application of risk management to medical devices*. The CD is being circulated for ballot and comment in ISO/TC 210 and for comment only in IEC/SC 62A under Mode 5 cooperation.

Please note the line number of the text that your comment addresses and include this as the first line in the column headers "Paragraph/Figure/Table" in the ISO comment form.

**ISO TC 210/SC N**

Date: 2003-03-07

**ISO/CD 14971**

ISO TC 210–IEC/SC 62A JWG 1

Secretariat: AAMI (for ANSI)

# Medical devices — Application of risk management to medical devices

*Dispositifs médicaux — Application de la gestion des risques aux dispositifs médicaux*

**Warning**

This document is not an ISO International Standard. It is distributed for review and comment. It is subject to change without notice and may not be referred to as an International Standard.

Recipients of this draft are invited to submit, with their comments, notification of any relevant patent rights of which they are aware and to provide supporting documentation.

Document type: International Standard
Document subtype:
Document stage: (30) Committee
Document language: E

R:\Committee Documents\iso210\TC 210\TC 210 register docs\N215.doc STD Version 2 1

# Contents

Page

## Tables



## Figures

# Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

In the field of risk management for medical devices, Technical Committee ISO/TC 210 and IEC/SC 62A have established a joint working group, JWG 1, *Application of risk management to medical devices*.

International Standard ISO 14971 was prepared by ISO/TC 210, *Quality management and corresponding general aspects for medical devices*, and Subcommittee IEC/SC 62A, *Common aspects of electrical equipment used in medical practice*.

This second edition of ISO 14971 cancels and replaces ISO 14971: 2000.

For purposes of future IEC maintenance, Subcommittee 62A has decided that this publication remains valid until 200x. At this date, Subcommittee 62A, in consultation with ISO/TC 210, will decide whether the publication will be

- reconfirmed,
- withdrawn,
- replaced by a revised edition, or
- amended.

Annexes A to K of this International Standard are for information only.

# Introduction

This International Standard should be regarded as a framework for effective management by the manufacturer of the risks associated with the use of medical devices. The requirements that it contains provide a framework within which experience, insight, and judgment are applied systematically to manage these risks.

This standard deals with risks, primarily to the patient, but also to the operator, other persons, other equipment and the environment.

As a general concept, activities in which an individual, organization, or government is involved can expose those or other stakeholders to hazards which can cause loss or damage of something they value. Risk management is a complex subject because each stakeholder places a different value on the probability of harm occurring and on the detriment that might be suffered on exposure to a hazard.

It is accepted that the concept of risk has two components:

a) the probability of occurrence of harm, that is, how often the harm can occur;

b) the consequences of that harm, that is, how severe it might be.

The acceptability of a risk to a stakeholder is influenced by these components and by the stakeholder's perception of the risk.

These concepts are particularly important in relation to medical devices because of the variety of stakeholders including medical practitioners, the organizations providing health care, governments, industry, patients, and members of the public.

All stakeholders need to understand that the use of a medical device entails some degree of risk. Factors affecting each stakeholder's perception of the risks include the socio-economic and educational background of the society concerned and the actual and perceived state of health of the patient. The way a risk is perceived also takes into account, for example, whether exposure to the risk seems to be involuntary, avoidable, from a man-made source, due to negligence, arising from a poorly understood cause, or directed at a vulnerable group within society. The decision to embark upon a clinical procedure utilizing a medical device requires the residual risks to be balanced against the anticipated benefits of the procedure. Such judgments should take into account the intended use/intended purpose, performance, and risks associated with the medical device, as well as the risks and benefits associated with the clinical procedure or the circumstances of use. Some of these judgments can be made only by a qualified medical practitioner with knowledge of the state of health of an individual patient or the patient's own opinion.

As one of the stakeholders, the manufacturer should make judgments relating to safety of a medical device, including the acceptability of risks, taking into account the generally accepted state of the art, in order to determine the probable suitability of a medical device to be placed on the market for its intended use/intended purpose. This International Standard specifies a process by which the manufacturer of a medical device can identify hazards associated with a medical device, estimate and evaluate the risks associated with those hazards, control those risks, and monitor the effectiveness of that control

For any particular medical device, other International Standards may require the application of specific methods for controlling risk.

Annex A describes the reasoning for establishing the various requirements in this edition of ISO 14971.

# Medical devices — Application of risk management to medical devices

## 1 Scope

This International Standard specifies a process by which a manufacturer can identify the hazards associated with medical devices, including *in vitro* diagnostic medical devices, estimate and evaluate the risks, control these risks, and monitor the effectiveness of the control.

The requirements of this International Standard are applicable to all stages of the life cycle of a medical device.

This International Standard does not apply to clinical judgments relating to the use of a medical device.

It does not specify acceptable risk levels.

This International Standard does not require that the manufacturer has a formal quality management system in place. However, risk management can be an integral part of a quality management system (see, for example, Table B.1).

## 2 Terms and definitions

For the purposes of this International Standard, the following terms and definitions apply:

**2.1**
**accompanying document**
document accompanying a medical device and containing important information for the user, operator, installer, or assembler of the medical device, particularly regarding safety

NOTE Based on IEC 60601-1 1988, definition 2.1.4.

**2.2**
**harm**
physical injury or damage to the health of people, or damage to property or the environment

[ISO/IEC Guide 51:1999, definition 3 1]

NOTE Negative effects such as:

— unwanted pregnancy due to failing contraceptive devices, or

— psychological damage directly linked to the device

can also be considered to be included in the definition of harm.

**2.3**
**hazard**
potential source of harm

[ISO/IEC Guide 51 1999, definition 3 5]

**2.4**
**hazardous situation**
circumstance in which people, property, or the environment are exposed to one or more hazard(s)

[ISO/IEC Guide 51:1999, definition 3.6]

**2.5**
**intended use/intended purpose**
use of a product, process, or service in accordance with the specifications, instructions, and information provided by the manufacturer

**2.6**
**manufacturer**
natural or legal person with responsibility for the design, manufacture, packaging, or labelling of a medical device, assembling a system, or adapting a medical device before it is placed on the market and/or put into service, regardless of whether these operations are carried out by that person himself or on his behalf by a third party

NOTE Attention is drawn to the fact that the provisions of national or regional regulations can apply to the definition of manufacturer.

**2.7**
**medical device**
any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of

— diagnosis, prevention, monitoring, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of or compensation for an injury,

— investigation, replacement, modification, or support of the anatomy or of a physiological process,

— supporting or sustaining life,

— control of conception,

— disinfection of medical devices,

— providing information for medical purposes by means of *in vitro* examination of specimens derived from the human body,

and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means

[ISO/FDIS 13485:200x, definition 3 7]

NOTE As used in this standard, the term medical device includes any accessory to a medical device.

**2.8**
**objective evidence**
data supporting the existence or verity of something

NOTE Objective evidence may be obtained through observation, measurement, test, or other means.

[ISO 9000: 2000, definition 3 8.1]

**2.9**
**post-production**
that part of the life cycle of the product after the design has been completed and the device has been manufactured and released (e.g , product launch, distribution, installation, product use, product changes, decommissioning and disposal)

**2.10**
**procedure**
specified way to carry out an activity or a process

[ISO 9000: 2000, definition 3.4.5]

**2.11**
**process**
set of interrelated or interacting activities which transforms inputs into outputs

[ISO 9000: 2000, definition 3.4.1]

**2.12**
**record**
document stating results achieved or providing evidence of activities performed

[ISO 9000: 2000, definition 3.7.6]

**2.13**
**residual risk**
risk remaining after risk control measures have been taken

NOTE ISO/IEC Guide 51:1999, definition 3.9 uses the term "protective measures" rather than "risk control measures." However, in the context of this standard, "protective measures" are only one option for controlling risk as described in 6.2

**2.14**
**risk**
combination of the probability of occurrence of harm and the severity of that harm

[ISO/IEC Guide 51:1999, definition 3 2]

**2.15**
**risk analysis**
systematic use of available information to identify hazards and to estimate the risk

[ISO/IEC Guide 51·1999, definition 3.10]

**2.16**
**risk assessment**
overall process comprising a risk analysis and a risk evaluation

[ISO/IEC Guide 51:1999, definition 3.12]

**2.17**
**risk control**
process in which decisions are made and risks are reduced to, or maintained within, specified levels

**2.18**
**risk evaluation**
process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk

**2.19**
**risk estimation**
process used to assign values to the probability of occurrence of harm and the severity of that harm

**2.20**
**risk management**
systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, and controlling risk

**2.21**
**risk management file**
set of all records and other documents that are produced by the risk management process

**2.22**
**safety**
freedom from unacceptable risk

[ISO/IEC Guide 51:1999, definition 3.1]

**2.23**
**verification**
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

NOTE 1 The term "verified" is used to designate the corresponding status

NOTE 2 Confirmation can comprise activities such as:
— performing alternative calculations;
— comparing a new design specification with a similar proven design specification;
— undertaking and demonstrations, and
— reviewing documents prior to issue.

[ISO 9000 2000, definition 3 8.4]

# 3 General requirements for risk management

NOTE Attention is drawn to the fact that the provisions of national or regional regulations can also apply to some of the requirements specified within clause 3.

## 3.1 Risk management process

The manufacturer shall establish and maintain a process for identifying hazards associated with a medical device, estimating and evaluating the associated risks, controlling these risks, and monitoring the effectiveness of the controls throughout the life cycle. This process shall be documented and shall include the following elements:

— risk analysis;

— risk evaluation;

— risk control; and

— post-production information.

Where a documented product realization process exists, it shall incorporate the appropriate parts of the risk management process.

NOTE 1 A documented product realization process can be used to deal with safety in a systematic manner, in particular to enable the early identification of hazards in complex systems and environments.

NOTE 2 These documents can form part of a manufacturer's quality management system (e.g ISO 13485) and these documents can be referenced in the risk management file

NOTE 3 A schematic representation of the risk management process is shown in Figure 1 for illustration. Annex C contains a more detailed overview of the steps in the risk management process, again for illustration.

Compliance is checked by inspection of appropriate documents.

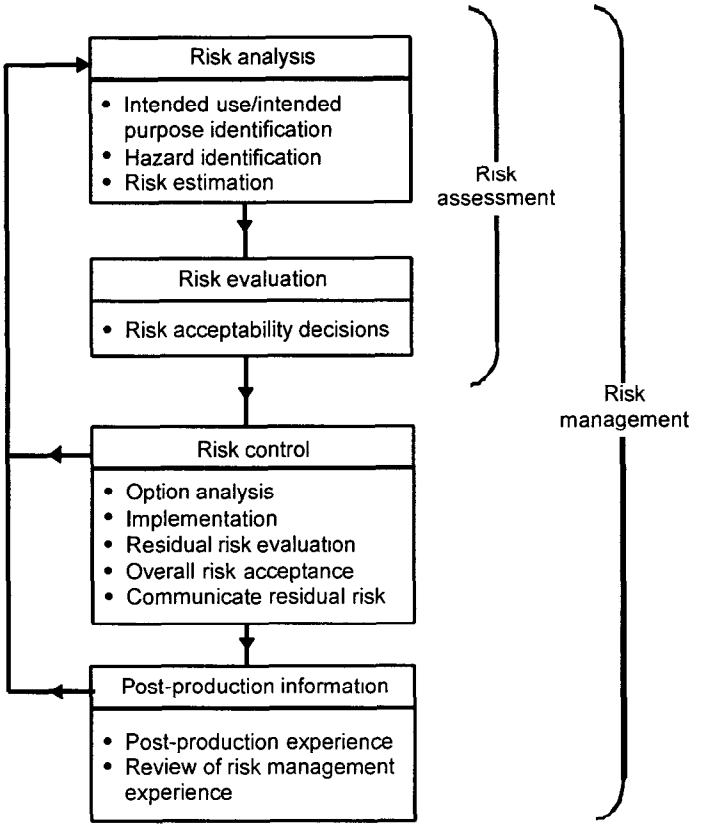



**Figure 1 — A schematic representation of the risk management process for illustration**

## 3.2 Management responsibilities

The manufacturer shall:

a) define the policy for determining acceptable risk, taking into account relevant International Standards and national or regional regulations;

b) ensure the provision of adequate resources;

c) ensure the assignment of qualified personnel (see 3.3) for management, performance of work and assessment activities; and

d) review the results of risk management activities at defined intervals to ensure continuing suitability and the effectiveness of the risk management process.

The above shall be documented.

NOTE The documents can form part of a manufacturer's quality management system (e g ISO 13485) and these documents can be referenced in the risk management file

Compliance is checked by inspection of the appropriate documents.

## 3.3 Qualification of personnel

The manufacturer shall ensure that those performing risk management tasks include persons with knowledge and experience appropriate to the tasks assigned to them. This shall include, where appropriate, knowledge and experience of the medical device (or similar devices) and its use and/or risk management techniques. Appropriate qualification records shall be maintained.

Compliance is checked by inspection of the appropriate records.

## 3.4 Risk management plan

For the particular medical device being considered, the manufacturer shall prepare a risk management plan in accordance with the risk management process. The risk management plan shall be part of the risk management file.

This plan for the particular medical device shall include at least the following:

a) The scope of the plan, identifying and describing the medical device and the life cycle phases for which each element of the plan is applicable;

b) verification activities;

c) assignment of responsibilities and authority;

d) requirements for review of risk management activities;

e) criteria for risk acceptability including criteria for accepting risks when the probability of occurrence of harm cannot be estimated; and

f) method of obtaining relevant post-production information.

NOTE 1 The criteria for risk acceptability will do much to determine the ultimate effectiveness of the risk management process. Refer to Annex D for guidance on establishing such criteria; refer to Annex E for guidance on developing a risk management plan.

NOTE 2 Not all parts of the plan need to be created at the same time, but can be developed over time. However, activities should be planned before they are undertaken.

If the plan changes during the life cycle of the medical device, a record of the changes shall be maintained in the risk management file.

Compliance is checked by inspection of the risk management file.

## 3.5 Risk management file

For the particular medical device being considered, the manufacturer shall establish and maintain a risk management file. In addition to the requirements of other clauses of this standard, the risk management file shall provide traceability for each hazard to:

— the risk analysis;

— the risk evaluation;

— the implementation and verification of the risk control measures; and

— the assessment that each residual risk(s) is acceptable.

NOTE 1 The records and other documents that make up the risk management file can form part of other documents and files required, for example, by a manufacturer's quality management system.

NOTE 2 The risk management file need not physically contain all the records and other documents relating to this International Standard However, it should contain at least references or pointers to all required documentation. The manufacturer should be able to assemble the information referenced in the risk management file in a timely fashion.

NOTE 3 The Risk management file can be in any form or type of medium.

# 4 Risk analysis

## 4.1 Risk analysis process

Risk analysis, as described in 4.2 to 4.4, shall be performed, and the conduct and results of the risk analysis shall be recorded in the risk management file.

NOTE 1 If a risk analysis or other relevant information is available for a similar medical device, it can be used as a starting point provided it can be demonstrated that the processes are similar or that the changes that have been made will not introduce significant differences in results. This should be based on a systematic evaluation of the changes and the ways they can influence the various hazards present.

NOTE 2 Some techniques that can be used for analysis of risks are described in Annex F.

In addition to the records required in 4.2 to 4.4, the documentation of the conduct and results of the risk analysis shall include at least the following:

a) a description and identification of the medical device that was analysed;

b) identification of the person(s) and organization which carried out the risk analysis;

c) date of the analysis.

Compliance is checked by inspection of the risk management file.

## 4.2 Intended use/intended purpose and identification of characteristics related to the safety of the medical device

For the particular medical device being considered, the manufacturer shall document the intended use/intended purpose and any reasonably foreseeable misuse. The manufacturer shall identify and document those qualitative and quantitative characteristics that could affect the safety of the medical device and, where appropriate, their defined limits (see Note 1). These documents shall be maintained in the risk management file.

NOTE 1 Annex G contains questions that can serve as a useful guide in drawing up such a list

NOTE 2 Additional guidance on risk analysis techniques for *in vitro* diagnostic medical devices is given in Annex H

NOTE 3 Additional guidance on risk analysis techniques for toxicological hazards is given in Annex I.

Compliance is checked by inspection of the risk management file.

## 4.3 Identification of known or foreseeable hazards

The manufacturer shall compile a list of known or foreseeable hazards associated with the medical device in both normal and fault conditions. Previously recognized hazards shall be identified. This list shall be maintained in the risk management file.

Foreseeable sequences of events that can result in a hazardous situation shall be considered and recorded.

NOTE 1 The examples of possible hazards listed in Annex J and in Annex H.2 for *in vitro* diagnostic medical devices can be used as a memory aid.

NOTE 2 To identify hazards not previously recognized, systematic methods covering the specific situation can be used (see Annex F)

Compliance is checked by inspection of the risk management file.

### 4.4 Estimation of the risk(s) for each hazard

For each identified hazard, the risk(s) in both normal and fault conditions shall be estimated using available information or data. For hazards for which the probability of the occurrence of harm cannot be estimated, at least a listing of the possible consequences of the hazard shall be prepared for use in Clause 6. The results of these activities shall be recorded in the risk management file.

Any system used for qualitative or quantitative categorization of probability of occurrence estimates or severity shall be recorded in the risk management file.

NOTE 1 Risk estimation incorporates an analysis of the probability of occurrence and the consequences. Depending on the area of application, only certain elements of the risk estimation process can need to be considered. For example, in some instances it will not be necessary to go beyond an initial hazard and consequence analysis.

NOTE 2 Risk estimation can be quantitative or qualitative. Methods of risk estimation, including those resulting from systematic faults, are described in AnnexD. Annex H.3 gives information useful for estimating risks for *in vitro* diagnostic medical devices.

NOTE 3 Some techniques that can be used for analysis of risks are described in annex E.

NOTE 4 Information or data for estimating risks can be obtained, for example, from:

- published standards;
- scientific technical data;
- field data from similar medical devices already in use including published reported incidents;
- usability tests employing typical users;
- clinical evidence;
- results of appropriate investigations;
- expert opinion; and
- external quality assessment schemes.

Compliance is checked by inspection of the risk management file.

## 5 Risk evaluation

For each identified hazard, the manufacturer shall decide, using the criteria defined in the risk management plan, whether the estimated risk(s) is so low that risk reduction need not be pursued. In this case, the requirements given in 6.2 to 6.6 do not apply for this hazard (i.e., proceed to 6.7). The results of this risk evaluation shall be recorded in the risk management file.

NOTE 1 Guidance for deciding on risk acceptability is given in Annex D 3

NOTE 2 Application of relevant standards as part of the medical device design criteria might constitute risk control activities, thus necessitating application of the requirements given in 6.3 to 6.6.

Compliance is checked by inspection of the risk management file.

# 6 Risk control

## 6.1 Risk reduction

When risk reduction is required, the manufacturer shall follow the procedure specified in 6.2 to 6.7 to control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable.

## 6.2 Option analysis

The manufacturer shall identify risk control measure(s) that are appropriate for reducing the risk(s) to an acceptable level.

Risk control shall consist of an integrated approach in which the manufacturer shall use one or more of the following in the priority order listed:

a) inherent safety by design;

b) protective measures in the medical device itself or in the manufacturing process;

c) information for safety.

NOTE 1 Measures of risk control can reduce the severity of the potential harm or reduce the probability of occurrence of the harm, or both.

NOTE 2 Technical standards address inherent, protective, and information for safety for many medical devices. These should be consulted as part of the risk management process. See also Table B.2.

The risk control measures selected shall be recorded in the risk management file.

If, during option analysis, the manufacturer determines that further risk reduction is not practicable, the manufacturer shall conduct a risk/benefit analysis of the residual risk (see 6.5); otherwise, the manufacturer shall proceed to implement the selected risk control measures.

Compliance is checked by inspection of the risk management file.

## 6.3 Implementation of risk control measure(s)

The manufacturer shall implement the risk control measure(s) selected in 6.2.

Implementation of the risk control measures shall be verified. This verification shall also be recorded in the risk management file.

The effectiveness of the risk control measures shall be verified and the results of the verification shall be recorded in the risk management file.

Compliance is checked by inspection of the risk management file.

## 6.4 Residual risk evaluation

Any residual risk that remains after the risk control measure(s) are applied shall be evaluated using the criteria defined in the risk management plan. The results of this evaluation shall be recorded in the risk management file.

If the residual risk does not meet these criteria, further risk control measures shall be applied (see 6.2).

For residual risks, which are judged acceptable, the manufacturer shall decide which information to put into the accompanying documents, in order to inform about the residual risk.

NOTE 1 National or regional regulatory requirements can apply.

NOTE 2 Guidance on communication of residual risk is found in Annex K.

Compliance is checked by inspection of the risk management file and the accompanying documents.

### 6.5 Risk/benefit analysis

If the residual risk is not judged acceptable using the criteria established in the risk management plan and further risk control is not practicable, the manufacturer shall gather and review data and literature on the medical benefits of the intended use/intended purpose to determine if they outweigh the residual risk. If this evidence does not support the conclusion that the medical benefits outweigh the residual risk, then the risk remains unacceptable. If the medical benefits outweigh the residual risk, then proceed to 6.6. Relevant information necessary to explain the residual risk shall be placed in the appropriate accompanying documents supplied by the manufacturer. The results of this evaluation shall be recorded in the risk management file.

Compliance is checked by inspection of the risk management file and the accompanying documents.

### 6.6 New hazards

The risk control measures shall be reviewed to identify if other hazards are introduced. If any new hazards are introduced by any risk control measures, the associated risk(s) shall be assessed (see 4.4). The results of this review shall be recorded in the risk management file.

Compliance is checked by inspection of the risk management file.

### 6.7 Completeness of risk control

The manufacturer shall assure that the risk(s) from all identified hazards have been considered. The results of this activity shall be recorded in the risk management file.

Compliance is checked by inspection of the risk management file.

## 7 Overall residual risk evaluation

After all risk control measures have been implemented and verified, the manufacturer shall decide if the overall residual risk posed by the medical device is acceptable using the criteria defined in the risk management plan.

If the overall residual risk is not judged acceptable using the criteria established in the risk management plan, the manufacturer shall gather and review data and literature on the medical benefits of the intended use/intended purpose to determine if they outweigh the overall residual risk. If this evidence supports the conclusion that the medical benefits outweigh the overall residual risk, then the overall residual risk can be judged acceptable. Otherwise, the overall residual risk remains unacceptable.

The overall residual risk evaluation shall be recorded in the risk management file.

Compliance is checked by inspection of the risk management file.

## 8 Risk management report

The risk management report shall:

— contain a summary of the results of the overall risk evaluation; and

435 — confirm that the risk assessment and risk control activities have been completed.

436 The risk management report shall be approved by the personnel assigned this responsibility and
437 authority.

438 The risk management report shall be included in the risk management file.

439 NOTE The risk management report can also summarize the risk assessment and risk control activities

440 Compliance is checked by inspection of the risk management file.

## 441 9 Production and post-production information

442 The manufacturer shall establish and maintain a documented feedback system to collect and review
443 information about the medical device or similar devices in the production and the post-production
444 phases. The information shall be evaluated for possible relevance to safety, especially the following:

445 a) if previously unrecognized hazards are present;

446 b) if the estimated risk(s) arising from a hazard is no longer acceptable; or

447 c) if the original assessment is otherwise invalidated.

448 If any of the above conditions occur:

449 — the impact on previously implemented risk management activities shall be evaluated and shall be
450 fed back as an input to the risk management process, and

451 — a review of the appropriate risk management file for the medical device shall be considered. If
452 there is a potential that the residual risk(s) or its acceptability has changed, the impact on
453 previously implemented risk control measures shall be evaluated.

454 The results of this evaluation shall be recorded in the risk management file.

455 NOTE 1 Some aspects of post-production monitoring are the subject of national or regional regulations. In
456 some cases, additional measures might be required (e.g., prospective post-production evaluations).

457 NOTE 2 See also 8.2 of ISO 13485:1200x.

458 NOTE 3 Information can be found at any stage of the medical device life cycle from inception to post-
459 production phases

460 Compliance is checked by inspection of the risk management file and other appropriate documents.

# Annex A
(informative)

# Rationale for requirements

## A.1 Introduction

The ISO/TC 210-IEC/SC 62A Joint Working Group 1, Application of risk management to medical devices, developed this rationale to document its reasoning for establishing the various requirements contained in ISO 14971. Those who make future revisions to the standard can use this document, along with experience gained in the use of the standard, to make the standard more useful to manufacturers, regulatory bodies, and health care providers.

A standard for the application of risk management to medical devices became important largely because of the increasing recognition by regulators that the manufacturer should apply risk management to medical devices. No medical device risk management standard existed, and this standard has been written to fill that gap. ISO TC 210 Working Group 4 was formed to develop the new standard. Almost simultaneously, drafters of the third edition of IEC 60601-1 planned to have risk management included in the standard then under development. They saw the need for a separate risk management activity and formed Working Group 15 of IEC/SC 62A. Recognizing that the efforts of these two working groups overlapped, IEC and ISO formed the Joint Working Group 1 (JWG1) on Risk Management combining the membership of both working groups. This collaboration resulted in the publication of ISO 14971 with both an ISO and an IEC logo. The dual logo signifies that both ISO and IEC recognize ISO 14971 as the international standard covering the application of risk management to medical devices.

When JWG1 started its discussions on the international risk management standard, there was no satisfactory standard in place to address risk management for medical devices. Crucial features of risk management needed to be addressed such as the process of risk evaluation, as well as the balancing of risks and benefits for medical devices. Manufacturers, regulatory bodies, and health care providers had recognized that "absolute safety" in medical devices was not achievable. In addition, the risks that derive from the increasing diversity of medical devices and their applications cannot be completely addressed through product safety standards. The recognition of these facts and the consequent need to manage risks from medical devices throughout their life cycle led to the decision to develop ISO 14971.

The JWG1's original plan was to write the standard in several parts, each dealing with a specific aspect of risk management. ISO 14971-1, covering risk analysis, was intended as the first part of an overall risk management standard. Later, the JWG1 decided that it was better to develop a single document that would include all aspects of risk management. The main reason for this was that it was apparent that risk management would be mandated by several regulatory regimes in the world, including Europe. It was therefore no longer useful or necessary to have a separate standard on risk analysis available. Also, making one risk management standard instead of having several parts would much better show the coherence between the several aspects of risk management.

In what follows, the numbering parallels the numbering of the various clauses and subclauses of ISO 14971

## A.2 Rationale for requirements in particular clauses and subclauses

### A.2.1 Scope

As explained in the introduction, a risk management standard applying to all medical devices is required. Risks exist throughout the product life cycle, and risks that become apparent at one point in the life cycle can be managed by action taken at a completely different point in the life cycle. For this reason, the JWG1 intended the standard to be a complete life cycle standard. This means that the standard instructs manufacturers to apply risk management principles to a medical device from its initial conception until its ultimate decommissioning and disposal.

The standard is not intended to apply to clinical decision making. The decision to embark upon a clinical procedure utilizing a medical device requires the residual risks to be balanced against the anticipated benefits of the procedure. Such judgements should take into account the intended use/intended purpose, performance, and risks associated with the medical device as well as the risks and benefits associated with the clinical procedure or the circumstances of use. Some of these judgements can be made only by a qualified health care professional with knowledge of the state of health of an individual patient and the patient's own opinion.

Although there has been significant debate over what constitutes an acceptable level of risk, the standard does not specify acceptability levels. The JWG1 believes that specifying a single level for acceptable risk would be inappropriate. This decision is based upon the belief that:

— the wide variety of devices and situations covered by the standard would make a single level meaningless; and

— local laws, customs, and values are more appropriate for defining risk acceptability for a particular culture or region of the world.

Because not all countries require a quality management system for medical device manufacturers, a quality management system is not required in the standard. However, the JWG1 believes that a quality management system is extremely helpful in managing risks properly. Because of this and because most medical device manufacturers do employ a quality management system, the standard is constructed so that it can easily be incorporated into the quality management system that they use. The relationship with ISO 13485: 200x is shown in Table B.1

### A.2.2 Terms and definitions

The JWG1 did not want to invent a host of new and possibly unfamiliar terms and so the standard is intentionally built upon the wealth of risk management information both in standards and in the literature. The JWG1 used existing definitions wherever possible for terms used in the standard. The primary sources for the definitions were:

— ISO/IEC Guide 51:1999, Guidelines for the inclusion of safety aspects in standards

— ISO 9001:2000, *Quality management systems—Requirements*

— ISO 13485:200x, *Medical devices—Quality management systems—System requirements for regulatory purposes*

The JWG1 also knew that risk management would be made mandatory, either explicitly or implicitly, by the European Union (EU), the United States, and other countries and regions of the world. The JWG1 therefore tried to use definitions that would be widely acceptable in a regulatory sense. For example, the term, "manufacturer" (subclause 2.6), while based on the medical device directive in the EU, is very consistent with the definition used in the United States. The term, "medical device" (subclause 2.7), was taken from ISO 13485 where a similar consideration for local regulations had also been applied. The combined term, "intended use/intended purpose" (subclause 2.5) is used because there is no consensus on which term to use. The Medical Device Directive uses "intended

purpose," whereas the United States regulations use "intended use." Both terms have essentially the same definition. The JWG1 decided to use the combined term along with a definition that is similar to that used in both the EU and the United States.

Only six other terms in ISO 14971 are not based on definitions in other standards. These are "post-production" (subclause 2.9), "risk control" (subclause 2.17), "risk evaluation" (subclause 2.18), risk estimation (subclause 2.19), "risk management" (subclause 2.20), and "risk management file" (subclause 2.21). A definition of "post-production" was added to emphasize that the entire life cycle of the device is important for risk management. The definitions for "risk control" and "risk evaluation" were provided to be consistent with the definitions of "risk analysis" given by ISO/IEC Guide 51. The definition for "risk management" emphasizes the use of a systematic approach and the need for management oversight. The concept of a "risk management file" was originally expressed in IEC 60601-1-4, but the JWG1 changed the definition because the definition in IEC 60601-1-4 refers to quality records, which need not exist for compliance with ISO 14971.

### A.2.3 General requirements for risk management

Although risk management activities are highly individual to the device being evaluated, there are basic elements that need to be included in the risk management process. This clause satisfies that need. This clause also allows for some differences in the requirements for meeting this standard, based on local differences in regulatory approaches.

World-wide applicability of this standard is important despite differing regional regulatory requirements. This note was needed so that both Europe and the United States (as well as other countries and regions) could use this standard in their regulatory programs. In Europe, manufacturers do not need to have a certified quality management system in place to meet the essential requirements necessary for applying a CE mark to their product. In the United States, a quality management system is always required to market a device (unless the device is specifically exempted). Subclauses 3.2 and 3.3 closely follow quality management system requirements. This note informs manufacturers that they can apply subclauses 3.2 and 3.3 in conjunction with a quality management system, when required by their local regulatory authorities.

#### A.2.3.1 Risk management process

This subclause requires each manufacturer to establish a risk management process as part of the design of a medical device. This is required so that the manufacturer can systematically ensure that the required elements are in the process. Risk Analysis, risk evaluation and risk control are commonly recognised as essential parts of risk management. In addition to these elements, the JWG1 wanted to emphasise, however, that the risk management process does not end with the design and manufacturing of a medical device, but continues on into the post-production phase. The JWG1, therefore, identified the gathering of post-production information as a required part of the risk management process. The JWG1 also believe that when a manufacturer employs a quality management system, the risk management process should be fully integrated into that quality management system.

#### A.2.3.2 Management responsibilities

The commitment of a manufacturer's management is critical for an effective risk management process. The JWG1 believes that these individuals should take responsibility for overall guidance of the risk management process. Therefore, the JWG1 included this subclause to emphasise their role. In particular the JWG1 concluded that:

a) Because this standard does not define acceptable risk levels, the manufacturer has to decide what criteria to apply, taking account of relevant factors;

b) In the absence of adequate resources, risk management activities would be less effective, even if complying with the letter of the other requirements of this standard;

c) Risk management is a specialized discipline and requires the use of individuals trained in risk management techniques (see rationale for 3.3); and

d) Risk management is an evolving process and periodic review of the risk management activities is needed to ascertain whether they are being carried out correctly, to rectify any weaknesses, to implement improvements, and to adapt to changes.

#### A.2.3.3 Qualification of personnel

The JWG1 believes it is most important to get qualified people to perform risk management tasks. The risk management process require people who know:

— how the device is constructed;

— how the device works;

— how the device is actually used; and

— how to apply the risk management process.

In general, this will require several experts, each contributing their specialist knowledge. Records of the appropriate qualifications are required to provide objective evidence. For confidentiality reasons, the standard does not require these records to be kept in the risk management file.

#### A.2.3.4 Risk management plan

A risk management plan is required because the JWG1 believes that:

— an organised approach is essential for good risk management

— the plan provides the roadmap for risk management; and

— the plan encourages objectivity and helps prevent essential elements being forgotten.

The elements a) to f) are required for the following reasons:

a) There are two distinct elements in the scope of the plan. The first identifies the intended medical device; the other identifies the phase of the life cycle covered by each element the plan. By defining the scope, the manufacturer establishes the baseline on which all the risk management activities are built.

b) Verification is an essential activity and is required by 6.3. Planning this activity helps ensure that essential resources are available when required. If verification is not planned, important parts of the verification could be neglected.

c) Allocation of responsibilities is needed to ensure that no responsibility is omitted.

d) This point is included as a generally recognised responsibility of Management.

e) The criteria for risk acceptability are fundamental to risk management and should be decided upon before risk analysis begins. This helps make the process in clause 5 be objective.

f) Device specific methods for obtaining post-market information need to be established so that there is a formal and appropriate way to feed back post-market information into the risk management process.

The requirement to keep a record of changes is to facilitate audit and review of the risk management process for a particular device.

### A.2.3.5 Risk management file

The standard uses this term to signify where the manufacturer can locate or find the locations of all the records applicable to risk management. This facilitates the risk management and enables more efficient auditing to this standard. Traceability is necessary to demonstrate that risk management process has been applied to each identified hazard.

## A.2.4 Risk analysis

The JWG1 used ISO 14971-1 as the basis for this section. This standard is the ISO version of EN 1441 on medical devices risk analysis and was made internationally available under the title *Medical Devices - Risk Management -Part 1: Application of Risk Analysis*. EN 1441 was written under a mandate of the European Commission, and gave the presumption of conformance with the requirements for risk analysis of the European medical device regulations.[1]

### A.2.4.1 Risk analysis process

The risk analysis process is described in subclauses 4.2, 4.3 and 4.4.

The JWG1 added a note on how to deal with the availability of a risk analysis for a similar medical device to inform users of the standard that when adequate information already exists it can and should be applied to save time, effort, and other resources. Users of the standard need to be careful, however, to assess systematically their previous work for applicability to the current risk analysis.

Note that details required by a), b), and c) form the basic minimum data set for ensuring traceability and are important for management reviews and for subsequent audits. The requirement in a) also helps clarify what is in the scope of the analysis and verify completeness.

### A.2.4.2 Intended use / intended purpose and identification of characteristics related to the safety of the medical device

This step forces the manufacturer to think about all the characteristics that could affect safety of the medical device. This analysis should include "reasonably foreseeable misuse." Devices are frequently used in situations other than those intended by the manufacturer and in situations other than those foreseen when a device is first conceived. It is important that the manufacturer tries to look into the future to see the hazards due to potential uses of their device.

Annex G is intended to be helpful in describing the characteristics of the medical device and the environments in which it is used. The JWG1 cannot emphasise too strongly that this list is not exhaustive. Every manufacturer should be creative in determining the relevant safety characteristics for the medical device under investigation. The list in Annex G was originally taken from ISO 14971-1 with some additions made as a result of comments on drafts of the standard. The list ought to stimulate thinking of 'where can things go wrong.' Annex H on *in vitro* devices and Annex I on toxicological hazards, have been taken from Annex A and Annex B of ISO 14971-1, respectively, with only minor changes.

### A.2.4.3 Identification of known or foreseeable hazards

This step requires that the manufacturer be systematic in the identification of potential hazards. The manufacturer should list "known or foreseeable hazards" based upon the safety characteristics identified in subclause 4.2. A risk can only be assessed and managed once a hazard has been identified. Listing the hazards allows this to be done systematically.

---

[1] EN 1441 was ratified on 13 September 1997 and its reference published in the European Community's Official Journal of 9 May 1998. The presumption of conformity with the essential requirements of the medical device directives will be withdrawn on 1 April 2004

Annex J is provided to help manufacturers identify hazards and contributing factors that can lead to unsafe conditions. An attempt is made in that annex to show the relationships between hazards, harms, hazardous situations and contributing factors. This is especially important when there is a sequence of events that in the end can lead to a hazardous situation. The manufacturer should recognise these sequences of events to address risk properly.

The list as given in Annex J is non-exhaustive and is not intended as a checklist, but rather to stimulate creative thinking.

Annex F is provided as guidance on common risk analysis techniques that can be helpful in the identification of hazards.

#### A.2.4.4 Estimation of the risks for each hazard

This is the final step of risk analysis. The difficulty of this step is that estimation of risk is different for every hazard that is under investigation as well as for every device. The JWG1 has therefore chosen to write the text of this subclause generically. Because hazards can occur both when the device functions normally and when the device malfunctions, one should look closely at both situations. In practice, both components of risk, probability and consequence, should be analysed separately. When a manufacturer uses a systematic way of categorising the severity levels or probability of occurrence of harm levels, the categorisation scheme should be defined and recorded in the risk management file. This enables the manufacturer to treat equivalent risks consistently and serves as evidence that the manufacturer has done so.

Some hazards occur because of systematic faults or initiating events. The probability of occurrence of harm is impossible to calculate. Such hazards must still be addressed and the JWG1 believes that listing such hazards separately would allow the manufacturer to focus on ameliorating the risks due these hazards.

Frequently, good quantitative data are not readily available. The JWG1 therefore has tried to avoid the suggestion that estimation of risk should be done only in a quantitative way.

The JWG1 provided Annex D as helpful guidance on risk analysis. The information originates from several sources, including IEC 60300:1995, *Dependability management – Part 3: Application guide – Section 9: Risk analysis of technological systems*. The JWG1 recognized the usefulness of IEC 60300 and extended it to apply to all medical devices and all phases of the risk management process. Although risk charts are used extensively in Annex D as examples, this standard does not require the use of risk charts.

### A.2.5 Risk Evaluation

Decisions have to be made about the acceptability of risk. A decision was placed at this point because this is the first occasion that the required information is available. Manufacturers can use the recently estimated risks and evaluate them using the criteria for risk acceptability defined in the risk management plan. They can screen the risks to determine which ones need to be reduced. Clause 5 was written in this way to allow the user of the standard to avoid unnecessary work.

### A.2.6 Risk Control

#### A.2.6.1 Risk reduction

The JWG1 intended that steps 6.2 to 6.7 make up a logical sequence of stages. This systematic approach is important since it ensures that relevant information is available when required.

#### A.2.6.2 Option analysis

Often there will be more than one way to reduce a risk. The three mechanisms listed:

— inherent safety by design;

— protective measures in the medical device itself or in the manufacturing process; and

— information for safety

are all standard risk reduction measures and are derived from ISO/IEC Guide 51. The priority order listed is important. This principle is found in several places, including IEC/TR 60513 and local or regional regulations (e.g., the European Medical Device Directive). If practicable, the device should be designed to be inherently safe. If this is not practicable, then protective measures such as barriers or audible alarms are appropriate. The least preferred protective measure is a written warning or contraindication.

The JWG1 recognised that one possible result of the option analysis could be that there is no practicable way for reducing the risk to acceptable levels according to the pre-established criteria for risk acceptability. For example, it could be impractical to design a life-supporting device with such an acceptable residual risk. In this case, a risk/benefit analysis can be carried out as described in subclause 6.5 to determine whether the benefit of the device to the patient outweighs the residual risk. This option is included at this point in the standard to make sure that every effort was first made to reduce risks to the pre-established acceptable levels.

#### A.2.6.3 Implementation of risk control measures

The JWG1 included two distinct verifications. The first verification is required to make sure that the risk control measure has been implemented in the final design. The second verification is required to ensure that measure as implemented actually reduces the risk.

#### A.2.6.4 Residual risk evaluation

A check was introduced here to determine whether the implemented measures have made the risk acceptable. If the risk is not less than the criteria established in the risk management plan, manufacturers are instructed to assess additional risk control measures. This iterative procedure should be continued until the risk is reduced to within the acceptability levels established in the risk management plan.

The JWG1 believes that the user should be provided with relevant information on residual risks so that the user can make informed decisions. However, it is the manufacturer's decision as to what and how much information on residual risk should be provided. This requirement is consistent with the approach taken in many countries and regions, including the United States and the European Union.

#### A.2.6.5 Risk/benefit analysis

There will be some occasions where the risk of a medical device is greater than would be generally accepted The JWG1 included this subclause to enable the manufacturer to provide a high-risk device for which they have done a careful evaluation and can show that the benefit of the device outweighs the risk.

#### A.2.6.6 Other generated hazards

The JWG1 included this subclause because it recognised that risk control measures alone or in combination might introduce a new and sometimes quite different hazard.

#### A.2.6.7 Completeness of risk evaluation

At this stage, the risk of all the hazards should have been evaluated. The JWG1 introduced this check to ensure that no hazards were left out in the intricacies of a complex risk analysis.

### A.2.7 Overall residual risk evaluation

During the process defined by clauses 4 through 6, manufacturers identify hazards, evaluate the risks, and implement risk control measures in their design one at a time. This is the point where the manufacturer has to step back, consider the combined impact of the individual residual risks, and make a decision as to whether to proceed with the device. It is possible that the overall residual risk can exceed the manufacturer's criteria for acceptable risk, even though individual residual risks do not. This is particularly true for complex systems and devices with a large number of risks. Even if the overall residual risk exceeds the criteria in the risk management plan, the manufacturer has one last opportunity to do an overall risk-benefit evaluation to determine whether a high risk, but highly beneficial, device should be marketed.

### A.2.8 Risk Management report

The risk management report is a crucial part of the risk management file. The JWG1 intended it to be a summary of the final results of the risk management process. The report serves as the high level document for all kinds of questions about risks associated with the device.

Completeness is very important in risk management. An incomplete task can mean that the risk of a hazard is not controlled and harm to someone can be the consequence. The problem can result from incompleteness at any stage of risk management, e.g., unidentified hazards, risks not assessed, unspecified risk control measures, or risk control measures not implemented. The risk management report is a tool to establish completeness of the risk management process by the requirement that it be approved by the person responsible for this task.

### A.2.9 Post-production information

The JWG1 cannot emphasize too often that risk management does not stop when the device goes into production. Risk management is an imperfect process because it starts based on an idea with no physical manifestation of the device. Risk estimates can be refined throughout the design process and made more accurate when a functioning prototype is built. Information for use in risk management can come from any source including production and other quality records. However, no amount of modeling can substitute for an actual device in the hands of actual users. This is where all the potential hazards become real. Because of this, manufacturers should monitor postmarket information for things that can affect their risk estimates and, therefore, their risk management decisions. This includes taking into account state of the art considerations and the practicability of applying these. With this post-production information the risk management process truly becomes a iterative closed-loop process.

# Annex B
(informative)

## Other standards that contain information related to the elements of risk management described in this International Standard

Table B.1 — Quality management elements that can be related to the elements of risk management

| Overview of the risk management process | | Subclauses of ISO 13485:200x [a] | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 4.1 (see note 1) | 4.2 (see note 2) | 5.1 | 5.2 | 5.3 | 5.4 | 5.5 | 5.6 | 6.1 | 6.2 | 6.3 | 6.4 | 7.1 | 7.2 | 7.3 | 7.4 | 7.5 | 7.6 |
| General requirements | | | | | | | | | | | | | | | | | | | |
| Risk analysis | Scope definition | | | | | | | | | | | | | | | | | | |
| | Hazard identification | | | | | | | | | | | | | | | | | | |
| | Risk estimation | | | | | | | | | | | | | | | | | | |
| Risk evaluation | | | | | | | | | | | | | | | | | | | |
| Risk control | Analysis of options | | | | | | | | | | | | | | | | | | |
| | Decision making | | | | | | | | | | | | | | | | | | |
| | Implementation | | | | | | | | | | | | | | | | | | |
| Post-production information | | | | | | | | | | | | | | | | | | | |

**Table B.1 — Quality management elements that can be related to the elements of risk management**

| Overview of the risk management process | | Subclauses of ISO 13485:200x [a] | | | | | |
|---|---|---|---|---|---|---|---|
| | | 8.1 | 8.2 | 8.3 | 8.4 | 8.5 | |
| General requirements | | | | | | ■ | |
| Risk analysis | Scope definition | | | | | | |
| | Hazard identification | | | | | | |
| | Risk estimation | ■ | ■ | | ■ | | |
| Risk evaluation | | | | | | | |
| Risk control | Analysis of options | | | | | | |
| | Decision making | | | | | | |
| | Implementation | | | | | | |
| Post-production information | | | | | | ■ | |

NOTE 1 Risk management can be part of a quality management system.

NOTE 2 The risk management file can include quality records.

[a] Shaded areas indicate the parts of the risk management process which might be related to this International Standard.

792

Table B.2 — Other International Standards that can be related to the elements of risk management

| Overview of the risk management process | | Applicable standards[a] | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ISO 9001 | ISO 9000-3 | ISO 10993-1 | ISO 13485 | ISO 14969 | IEC 60300-3-9 | IEC/TR 60513 | IEC 60601-1-4 | IEC 60812 | IEC 61025 | EN 12442-1 |
| | Scope definition | | | | | | | | | | | |
| Risk analysis | Hazard identification | | | | | | | | | | | |
| | Risk estimation | | | | | | | | | | | |
| Risk evaluation | | | | | | | | | | | | |
| | Analysis of options | | | | | | | | | | | |
| Risk control | Decision making | | | | | | | | | | | |
| | Implementation | | | | | | | | | | | |
| Post-production information | | | | | | | | | | | | |

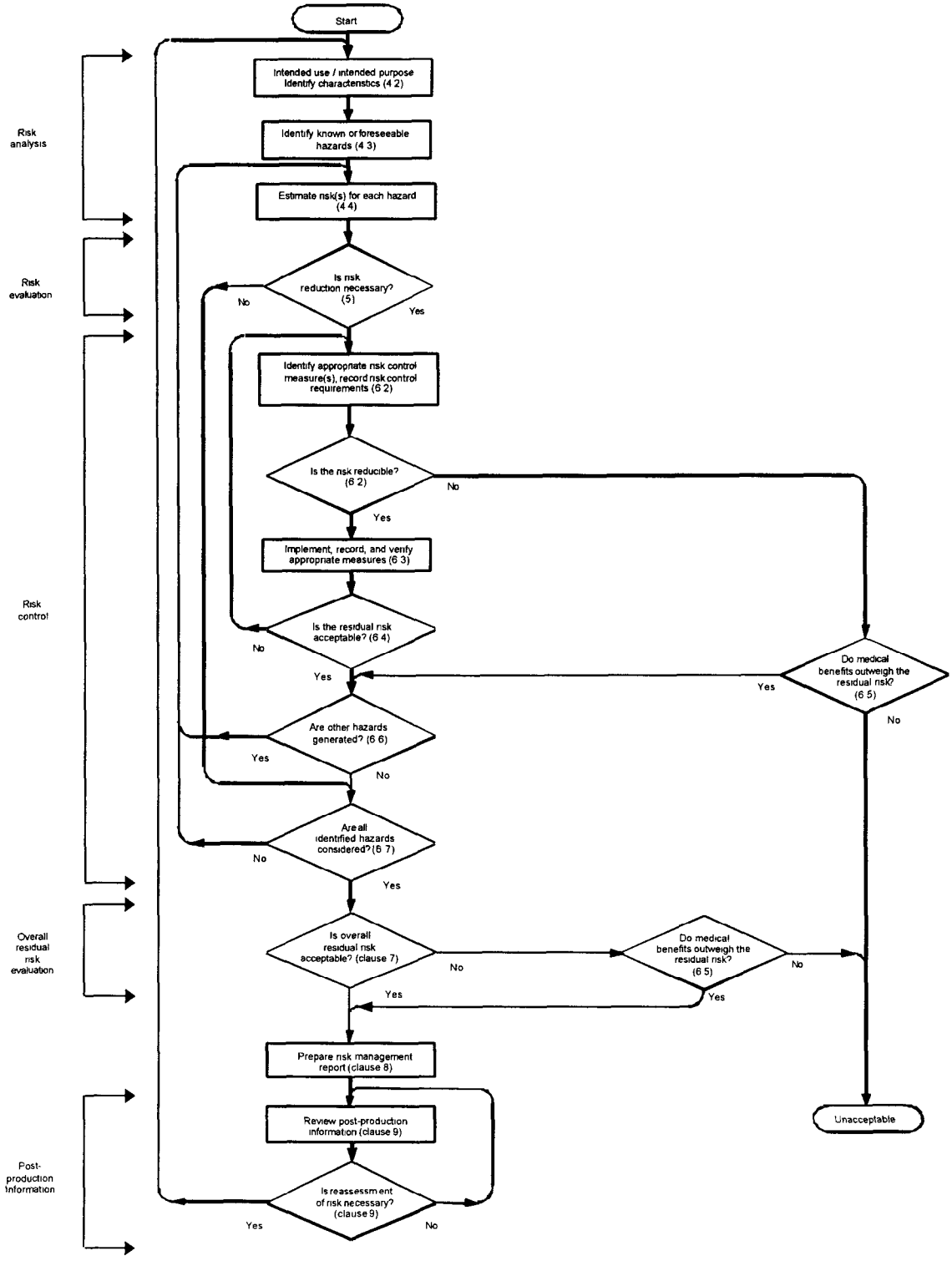
[a] Shaded areas indicate the parts of the risk management process which might be related to these International Standards

# Annex C
(informative)

## Overview of the risk management process for medical devices

Figure C.1 is provided to give the user of this standard an overview of the risk management process. It is for illustrative purpose only.

Figure C.1 is an expansion of the mechanism provided in this International Standard. As indicated in Figure C.1, the process needs to be iterative, covering each risk in turn, and returning to earlier steps if risk control measures introduce new hazards or if new information becomes available.




802
803

804 **Figure C.1 — Overview of risk management activities as applied to medical devices**

# Annex D
(informative)

# Risk concepts applied to medical devices

## D.1 Initiating Causes

### D.1.1 Initiating causes for electromedical devices—faults

A hazardous situation can result from the fault of an electromedical system. There are two possible types of fault:

— random faults, and

— systematic faults.

#### D.1.1.1 Random faults

For many events, a statistical probability of fault can be assigned (e.g., the probability of fault of an assembly is often estimated from the fault probabilities of the components which make up the assembly). In this case, a numerical value can be given for the probability of the fault. It is usually assumed here that such faults are random in nature.

#### D.1.1.2 Systematic faults

Systematic faults are due to errors (including errors of commission and omission) in any activity that, under some particular combination of inputs or environmental conditions, will permit a fault.

Errors leading to systematic faults can occur in both hardware and software and can be introduced at any time during a medical device's development, manufacture, or maintenance. Some examples of systematic faults are:

a) An incorrectly rated fuse fails to prevent a hazardous situation. The fuse rating might have been incorrectly specified, incorrectly fitted during manufacture, or incorrectly replaced during repair.

b) A software database does not provide for the condition of full database. If the database is full, it is not clear what the software will do. A possible consequence is that the system will delete existing records to make room for new ones.

The accurate estimation of systematic fault rates is difficult. This occurs primarily for the two following reasons:

a) Systematic fault rates are laborious and expensive to measure. Achieving a reasonable level of confidence in the result will not be possible without a long history of measuring fault rates.

b) Consensus does not exist for a method of estimating systematic fault rates quantitatively

In cases where an appropriate level of confidence cannot be established for estimating systematic faults, the risk should be managed based on the severity of the harm resulting from the hazard. Initially, risk estimation for systematic faults should be based on the presumption that the systematic fault will occur at an unacceptable rate

It is important to observe that there is an inverse relationship between the rigor of the development processes used to design complex systems and the possibility of a systematic fault being introduced or remaining undetected. It is often appropriate to determine the required rigor of the development process by taking account of the severity of the consequence of the systematic faults and the effect of risk-control measures external to the device. The worse the consequence and the less the effect of external risk-control measures, the higher the required rigor of the development process.

### D.1.2 Initiating causes for non-electromedical devices

The concepts of initiating causes that are random or systematic also apply, in a sense, to non-electromedical devices. For example, the presence of infectious or toxic substances in or on a medical device can sometimes be described by a probability distribution and would be treated in the same way as a random fault for hardware. In other cases, the presence of the offending material can better be characterized as systematic. This would be the case for example with:

— novel hazards that are poorly understood such as BSE transmission; or

— toxic agents for which one cannot determine a threshold below which toxic effects do not occur.

In these cases, analogously to systematic faults for electromedical devices, probabilities cannot be estimated.

## D.2 Risk estimation

Various methods can be used to estimate risk. While this International Standard does not require that a particular method be used, it does require that risk estimation be carried out (see 4.4). Quantitative risk estimation is possible when suitable data are available. Methods for quantitative risk estimation could merely result from the adaptation of a qualitative method, or an alternative approach might be appropriate.

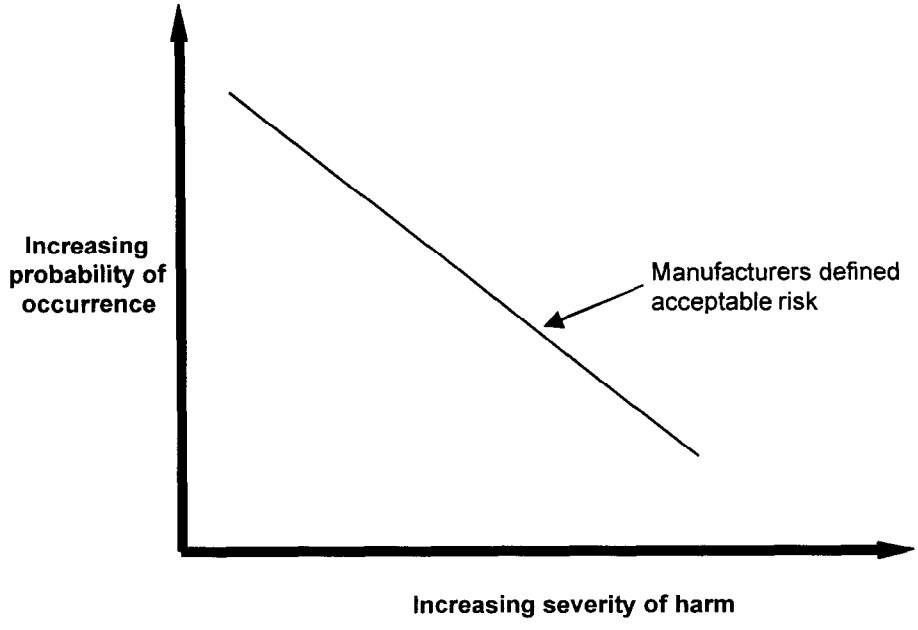
A risk chart such as shown in Figure D.1 can be used to help define risk. Use of such a three-region risk chart based on Figure D.1 will be used in examples throughout this annex. This does not imply that this method has general applicability to medical devices, however, it can be useful in many instances. If a risk chart approach is used for estimating risk, the particular risk chart and the interpretation used should be justified for that application.

The concept of risk is the combination of the following two components:

— the probability of occurrence of harm, that is, how often the harm can occur; and

— the consequences of that harm, that is, how severe it might be.

Risk estimation should examine the initiating events or circumstances, the sequence of events that are of concern, any mitigating features, and the nature and frequency of the possible deleterious consequences of the identified hazards. Risk should be expressed in terms that facilitate risk control decision-making. In order to analyze risks, their components, i.e., probability and severity, should be analyzed separately.




875

876 **Figure D.1 — Example of a risk chart**

877 ## D.2.1 Probability

878 ### D.2.1.1 Probability estimation

879 In appropriate situations where sufficient data are available, a quantitative categorization of probability
880 levels is preferred. If this is not possible, the manufacturer should give a qualitative description. A
881 qualitatively good description is preferable to quantitative inaccuracy. For a qualitative categorization
882 of probability levels, the manufacturer can use descriptors appropriate for the medical device. The
883 concept is in reality a continuum, however, in practice a number of discrete levels can be used. In this
884 case, the manufacturer decides how many categories are needed and how they are to be defined.
885 The levels can be descriptive (e.g., incredible, improbable, remote, occasional, probable, frequent) or
886 symbolic (P1, P2, etc.).

887 Probability estimation examines the initiating events or circumstances and the sequence of events that
888 are of concern. This includes answering the following questions.

889 — Does the hazard occur in the absence of a failure?

890 — Does the hazard occur in a fault condition?

891 — Does the hazard occur only in a multiple-fault condition?

892 Three approaches are commonly employed to estimate probabilities:

893 — use of relevant historical data;

894 — prediction of probabilities using analytical or simulation techniques; or

895 — use of expert judgment.

All these approaches can be used individually or jointly. The first two approaches are complementary; each has strength where the other has weaknesses. Wherever possible, both should be used. In this way, they work as independent checks on each other, and this might serve to increase confidence in the results. When these two approaches cannot be used or are not sufficient, it might be necessary to rely on expert judgment.

#### D.2.1.2 Risks whose probability cannot be estimated

Confidence in a risk estimate is enhanced when a quantitative estimate of the probability of occurrence can be made on the basis of precise and reliable data or when reasonable qualitative estimates are possible. However, this is not always the case. For example, the probability of systematic faults, such as those discussed in E.1.1.2, are extremely difficult to estimate. When the accuracy of the probability estimate is in doubt, it is often possible to establish a broad range for the probability, or determine that it is no worse than some particular value. Examples where risks cannot be estimated include:

— the risk of software failure; or

— very rare situations, such as terrorist activity, aeroplane disasters or, more relevantly, malicious misuse of a medical device.

In such cases, the risk estimate should be made on the basis of a reasonable worst-case estimate of probability. In some instances, it is convenient to set this default value of the probability to one and to base risk control measures on preventing the hazard entirely or in reducing the severity of the harm (see D.3).

Some examples for non-electromedical devices where it may not be possible to make any estimate of the probability of a risk occurring include:

— novel hazards that are poorly understood, e.g., imprecise knowledge of the infectivity of the causative agent of BSE prevents quantification of the risk of transmission; or

— certain toxicological hazards, such as genotoxic carcinogens and sensitising agents, where it is not possible to determine a threshold of exposure below which toxic effects do not occur.

For such hazards, the probability of harm occurring at a particular level of exposure cannot be estimated on the basis of scientific data. In the absence of any data on the probability of occurrence of harm, it is not possible to reach any risk estimate and it is therefore necessary to evaluate the risk on the basis of the nature of the hazard alone. If it can be concluded that the hazard is of little practical consequence, the risk can be classified as broadly acceptable and no risk control measures are necessary. However, for significant hazards, in other words hazards which could inflict harm of very high severity, such as those noted above, no level of exposure can be identified that corresponds to a risk so low that there is no need to bother about it. In that case, we acknowledge that we are really addressing the consequence of the hazard. It is therefore necessary to implement risk control measures to ensure that the consequence and risk is as low as is reasonably practicable. It is also necessary to include warnings in respect of such risks in the accompanying documents.

### D.2.2 Severity levels

To categorize the levels of severity, the manufacturer should use descriptors appropriate for the medical device. The concept of severity levels is, in reality, a continuum, however, in practice, one usually chooses a small number of discrete levels. In such cases, the manufacturer decides how many categories are needed and how they are to be defined. The levels can be descriptive (e.g., negligible, marginal, critical, serious, catastrophic) or symbolic (S1, S2, etc.). See the examples in D.2 3.

These levels will need to be customized by the manufacturer for a particular medical device considering both short-term and long-term effects and when used should be clearly defined.

### D.2.3 Examples

Sufficient data are not always available to perform an objective quantitative analysis. When quantitative analysis is not possible, qualitative or semi-quantitative analyses can be appropriate. The manufacturer should carefully define severity levels and probability levels appropriate to the device being analyzed before initiating the risk estimation process.

#### D.2.3.1 Qualitative analyses

Several approaches can be used for qualitative analysis. A typical approach is to use an N-by-M matrix to describe the probabilities and severities of the risk associated with each hazard. One carefully defines N levels of probability and M levels of severity. Each cell of the matrix represents a single combination of probability and severity. A simple example is a 3X 3 matrix based upon the definitions in Table D.1 and Table D.2.

**Table D.1 — Qualitative Severity Levels**

| Severity | Definition |
|---|---|
| Significant | Death or loss of function or structure |
| Moderate | Reversible or minor injury |
| Negligible | Will not cause injure or will injury slightly |

**Table D.2 — Qualitative Probability Levels**

| Probability | Definition |
|---|---|
| High | Likely to happen, often, frequent |
| Medium | Can happen, but not frequently |
| Low | Unlikely to happen, rare, remote |

Each of the locations in the matrix is initially identified as acceptable or unacceptable using the manufacturer's risk acceptability criteria. The result is shown in Figure D.2.

| | | Qualitative Severity Levels | | |
|---|---|---|---|---|
| | | **Negligible** | **Moderate** | **Significant** |
| **Qualitative Probability Levels** | **High** | Unacceptable | Unacceptable | Unacceptable |
| | **Medium** | Acceptable | Acceptable | Unacceptable |
| | **Low** | Acceptable | Acceptable | Acceptable |

**Figure D.2 — Example of a 3 x 3 risk matrix of qualitative analysis**

#### D.2.3.2 Semi-Quantitative Analysis

Here is an example of a semi-quantitative analysis. It is semi-quantitative because only the probability levels are quantified and comparable. Judgments are made on the relative values for the severity levels, but no attempt is made to provide a numeric scale. In practice, few risk analyses will be done quantitatively because of the difficulty in comparing the value of a death to, say, a successful surgical intervention.

In this example, a 5 x 5 matrix is used. The levels of probability and severity are defined in Table D.3 and Table D.4.

**Table D.3 — Example of Semi-quantitative Severity Levels**

| Severity | Definition |
|---|---|
| Catastrophic | Results in patient death |
| Critical | Results in permanent impairment or life-threatening injury |
| Serious | Medical intervention required to prevent permanent impairment or permanent damage to a body structure |
| Minor | Minor injury or temporary impairment not requiring medical intervention |
| Negligible | Inconvenience or temporary discomfort |

**Table D.4 — Example of Semi-Quantitative Probability Levels**

| Probability | Definition |
|---|---|
| Frequent | >10% (10 occurrences in 100 opportunities/uses/products) |
| Probable | 1% to 10% |
| Occasional | 0.1% to 1% |
| Remote | .0001% to 0.1% |
| Improbable | <.0001% |

The definitions for probability can be different for different product families. For example, a firm can choose to use one set of definitions for X-ray machines, but can have a different set of definitions for sterile disposable dressings. Thus, as noted in Table D.4, the rates of occurrence can represent failures per use of a multiple-use device or percentage of units of a disposable device that fail.

One can use "likelihood of detection" criteria to help quantify the "probability of occurrence". In this instance, the "likelihood of detection" would be a factor in determining the "probability of occurrence." The "likelihood of detection" statistic typically is utilized with complex electronic products or complex multi-step processes.

Implicit in the consideration of the probability of occurrence is the concept of patient exposure. If there is no probability of exposure of a hazard to a patient, there is no harm. Therefore the rate of occurrence should take into consideration the level or extent of exposure to the patient.

There are several significant statistics that are important for analyzing the probability of occurrence. These statistics include, but are not limited to, the following:

— How often is a particular device is used?

— What is the lifetime of the device?

— Who makes up the user and patient populations?

— What is the number of users/patients?

— How long and under what circumstances is the user/patient exposed?

The next step is to overlay the various levels of severity and probability of occurrence onto a risk table or risk chart with the results of applying the manufacturer's risk acceptability criteria.

An example of a three-region risk table for a 5 x 5 quantitative analysis is shown in Figure D.3.

| | | Semi-quantitative Severity Levels | | | | |
|---|---|---|---|---|---|---|
| | | **Negligible** | **Minor** | **Major** | **Critical** | **Catastrophic** |
| **Semi-Quantitative Probability Levels** | **Frequent** | Unacceptable | Unacceptable | Unacceptable | Unacceptable | Unacceptable |
| | **Probable** | Acceptable | Unacceptable | Unacceptable | Unacceptable | Unacceptable |
| | **Occasional** | Acceptable | Acceptable | Acceptable | Unacceptable | Unacceptable |
| | **Remote** | Acceptable | Acceptable | Acceptable | Unacceptable | Unacceptable |
| | **Improbable** | Acceptable | Acceptable | Acceptable | Acceptable | Acceptable |

**Figure D.3 — Example of a semi-quantitative analysis**

Other matrices besides 5x 5 can be utilized; however, matrices higher than 5x 5 (such as 10 x 10) can require significantly more data to be able to meaningfully distinguish between the various levels. Rationales for all choices should be documented as appropriate. While the above examples were 3 x 3 and 5x 5, there is no requirement that these matrices be balanced. For example, a 4x 5 matrix may be appropriate for a given application.

## D.3 Risk acceptability

This International Standard does not specify acceptable risk. That decision is left to the manufacturer. Methods of determining acceptable risk include the following:

— using applicable standards that specify requirements which, if implemented, will indicate achievement of acceptability concerning particular kinds of medical devices or particular risks;

— following appropriate guidance, for example, that obtained by using the single-fault philosophy (for details, see 9.10 of IEC/TR 60513:1994); or

— comparing levels of risk evident from medical devices already in use.

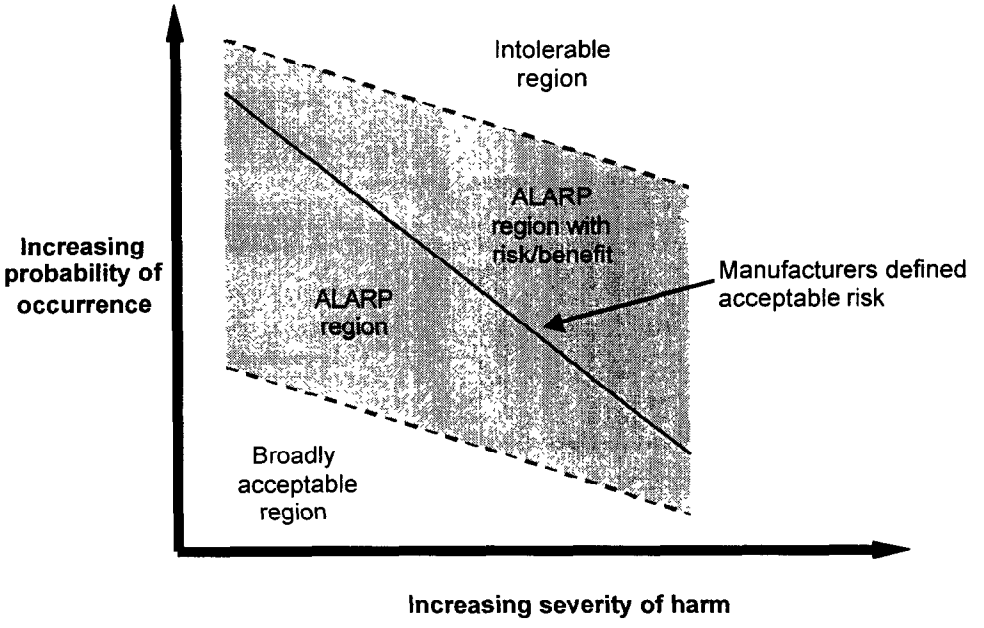
It is frequently convenient to categorize risks into the following three regions:

— the broadly acceptable region;

— the ALARP (As Low As Reasonably Practicable) region; and

— the intolerable region.

This three-region concept of risk is illustrated in Figure D.4. The definition of these regions will need to be customized for a particular medical device. The acceptable risk defined by the manufacturer is shown for comparison.




1011

1012 **Figure D.4 — Example of a three-region risk chart**

1013 ### D.3.1 Broadly acceptable region

1014 In some cases, a risk is so low that it is negligible in comparison with other risks. Such risks are called
1015 broadly acceptable, and risk control need not be actively pursued.

1016 ### D.3.2 ALARP region

1017 It might be thought that any risk associated with a medical device would be acceptable if the patient's
1018 prognosis were improved. This cannot be used as a rationale for the acceptance of unnecessary risk.
1019 All risks should be reduced to the lowest level practicable, bearing in mind the state of the art and the
1020 benefits of accepting the risk and the practicability of further reduction.

1021 "State of the art" is used here to mean what is currently and generally accepted as good practice.
1022 Various methods can be used to determine "state of the art" for a particular device. Examples are:

1023 — standards used for the same or similar devices;

1024 — best practices as used in other devices of the same or similar type; or

1025 — results of accepted scientific research.

1026 State of the art does not mean the most technologically advanced solution.

1027 Practicability refers to the ability of a manufacturer to reduce the risk. Practicability has two
1028 components:

1029 — technical practicability, and

1030 — economic practicability.

Technical practicability refers to the ability to reduce the risk regardless of cost. The following are a few examples where technical practicality is questionable:

— Including so many warning/caution labels that the user is hampered in operating the medical device.

— Multiple alarms that create confusion.

— Communicating too many residual risks so that the operator has difficulty understanding which ones are really important.

— Overly complex procedures for using the medical device so that the intended use/intended purpose is compromised.

— Using risk control measures that compromise the intended use/intended purpose (e.g., reducing the power of an electrosurgical unit below a level to be effective).

Economic practicability refers to the ability to reduce the risk without making the provision of the medical device an unsound economic proposition. Cost and availability implications are considered in deciding what is practicable to the extent that these impact upon the preservation, promotion, or improvement of human health.

Major risks should normally be reduced even at considerable cost. Near the broadly acceptable region, a balance between risk and benefit can suffice.

### D.3.3 Intolerable region

Some risks, if they cannot be reduced, can always be judged intolerable.

### D.3.4 Risk-acceptability decisions

There is an important distinction to be made between risks that are so low that there is no need to consider them and risks which are greater than that but which we are prepared to live with because of the associated benefits and the impracticality of reducing the risks. When a hazard has been identified and the risk estimated, the first question to be asked is whether the risk is already so low that there is no need to consider it and therefore no need to progress to risk reduction. This decision is made once for each hazard.

If the decision at the first stage is that the risk is not so low that there is no need to consider it, the next stage is to progress to risk reduction. Risk reduction might or might not be practicable, but it should be considered. The possible outcomes of this second stage are as follows:

— That one or more risk-reduction measures bring the risk down to a level where it is not necessary to consider it further; or

— That, whether or not some risk reduction is possible, reducing the risk down to the "no need to consider it" level is not practicable.

In the latter case, the risk should be reduced to a level as low as reasonably practicable (ALARP). Any residual risk that remains after the risk control measures are applied should be evaluated using the criteria defined in the risk management plan. If a risk is still judged not acceptable, a risk/benefit analysis can be carried out (see D.5).

Finally, once all risks have been found to be acceptable, the overall residual risk is evaluated (see D.6) to assure that the risk/benefit balance is still maintained (see D.5).

Thus, there are three decision points in the process, where different questions are asked about the acceptability of risks:

a) Whether the risk is so low that there is no need to consider it?

b) Whether there is no longer any reason to consider the risk, or the risk is as low as is reasonably practicable and outweighed by the benefit?

c) Whether the overall balance of all the risks with all the benefits is acceptable?

Risks, for which the probability cannot be estimated, have to be reduced to a level as low as reasonably practicable.

## D.4 Risk Control

### D.4.1 Option Analysis

Once it has been determined that a risk must be reduced, the designer/engineer is faced with options on how to do it. The following is a non-exhaustive list of risk control approaches that are typically used:

— Designing for inherent safety, e.g., eliminating a particular hazard or reducing the severity of the consequences. Typical techniques are designing out the hazard itself, designing in redundancy, using automatic cut-offs or safety valves, use of high integrity components, etc.

— Implementing protective measures such as alarms to alert the user/operator to hazardous conditions.

— Implementing control measures in the manufacturing process, e.g., to improve the tolerances of components that are causes for failure modes.

— Providing training for the user/operator to improve their performance or their capability in detecting errors.

— Communicating warnings about improper use, hazards that can occur, or other information that can help to reduce risk.

— Specifying adequate administrative protective measures, e.g., necessary maintenance and maintenance intervals, maximum expected product service life, or how to dispose of the device properly.

— Implementing post-production monitoring of specific endpoints.

Generally speaking, the options in the above list are ordered with regard to their effectiveness in reducing risk. The design team should take this into account before decisions are made on which combination of measures will be used.

### D.4.2 Risk Control Examples

Table D.5 lists some examples of risk control measures that are commonly used. The decision to use any of these measures is product and process specific Some of the examples have general applicability.

**Table D.5 — Some Examples of Risk Control Measures**

| Product /Process | Safe Design | Protective Measure | Risk Communication |
|---|---|---|---|
| Single Use Device | Self destruction after use | Obvious indication after 1st use | Warning for consequence(s) of reuse |
| Implants | Biocompatible and non-corrosive materials | Audible alarms when reaching critical limit(s) | Certification of user training |
| Software | Use of different algorithms for same decision | Software handshake to double check actual versus expected information | Screen user warnings |
| Packaging | Non-porous pouch material | Reinforced pinch point | Warning on product expiration, storage conditions, etc. |
| Sterilization | Design for "false-positive" free | E-Beam dose mapping | Visual aids for CCP |
| *In Vitro* Diagnostics | Design for "false-positive" free | Daily calibrations | Warning for false-positive or false-negative consequence(s) |

### D.4.3 Manufacturing Processes and Risk Control

Some hazards can be controlled most effectively by careful attention to the manufacturing process. This occurs where close tolerances of particular components are critical or where the manufacturing process itself can introduce hazards such as residues or unwanted particulates (see F.6). In such instances, techniques such as Hazard Analysis of Critical Control Points (HACCP) can be useful. The literature on this technique is extensive and references are provided in the bibliography.

## D.5 Risk/benefit analysis

The decision on whether risks are outweighed by benefits is essentially a matter of judgment by experienced and knowledgeable individuals. This standard explains how risks can be characterized so that a risk estimate can be determined with confidence. Unfortunately, there is no standardized approach to estimate benefit, and a greater degree of variation will be the inevitable result of using different approaches and of the greater subjectivity involved.

In this standard, a risk benefit analysis is only permitted to justify a high risk once all practicable measures to reduce the risk have been applied. If, after applying these measures, the risk is still not judged acceptable using the criteria in the risk management plan, a risk benefit analysis is needed to establish whether the device is likely to provide more benefit than harm.

The benefit arising from a medical device is related to the likelihood and extent of the improvement of health expected from its use, judged in relation to the outcome expected from alternative treatment options. Benefit can be estimated from knowledge of:

— the performance expected during clinical use;

— the clinical outcome expected from that performance, and

— factors relevant to the risks and benefits of other treatment options.

Confidence in the benefit estimate is strongly dependent on the reliability of evidence addressing these factors.

An estimate of clinical benefit can vary markedly between different stages of the design cycle. If reliable clinical data demonstrating the consistent performance and efficacy of the product are available, the clinical benefit can be estimated confidently. In cases where clinical data are limited in

quantity or quality, benefit must be estimated with greater uncertainty from whatever relevant information is available. For example, it is sometimes necessary early in the process to estimate the expected degree of improvement to health from the design intention; however, in the absence of relevant clinical data, the likelihood of achieving the intended performance and the desired clinical effect will have to be predicted by reference to quality assurance measures and *in vitro* or *in vivo* performance characteristics.

Where significant risks are present, and there is a high degree of uncertainty in the benefit estimate, it will be necessary to verify the anticipated performance and/or efficacy as soon as possible through clinical investigation. This is essential to confirm that the risk/benefit balance is as expected and to prevent unwarranted exposure of patients to a large residual risk.

### D.5.1 Risk evaluation depends on multiple criteria.

Those involved in making such judgments have a responsibility to understand and take into account the technical, clinical, regulatory, economic, sociological and political context of their risk management decisions. This can involve an interpretation of fundamental requirements set out in applicable regulations or standards, as they apply to the product in question under the anticipated conditions of use. Since this type of analysis is highly product specific, further guidance of a general nature is not possible. Instead, the safety requirements specified by standards addressing specific products or risks can be presumed to be consistent with an acceptable level of risk, especially where the use of those standards is sanctioned by the prevailing regulatory system. Note that a clinical investigation, in accordance with a legally recognised procedure, might be required to ensure that the balance between medical benefit and residual risk is acceptable.

### D.5.2 A Rigorous Approach to a Risk Benefit Comparison

A comparison of risks and benefits is only possible if a common scale is used for both variables. There are several ways that this can be accomplished, the example below being one of them. Making quantitative estimates is usually extremely difficult, and one frequently must rely on a qualitative analysis.

An example of an approach to making "benefit" and "risk" directly comparable for a therapeutic device is illustrated in Figure D.5. This example illustrates some of the difficulties that must be addressed in practice.

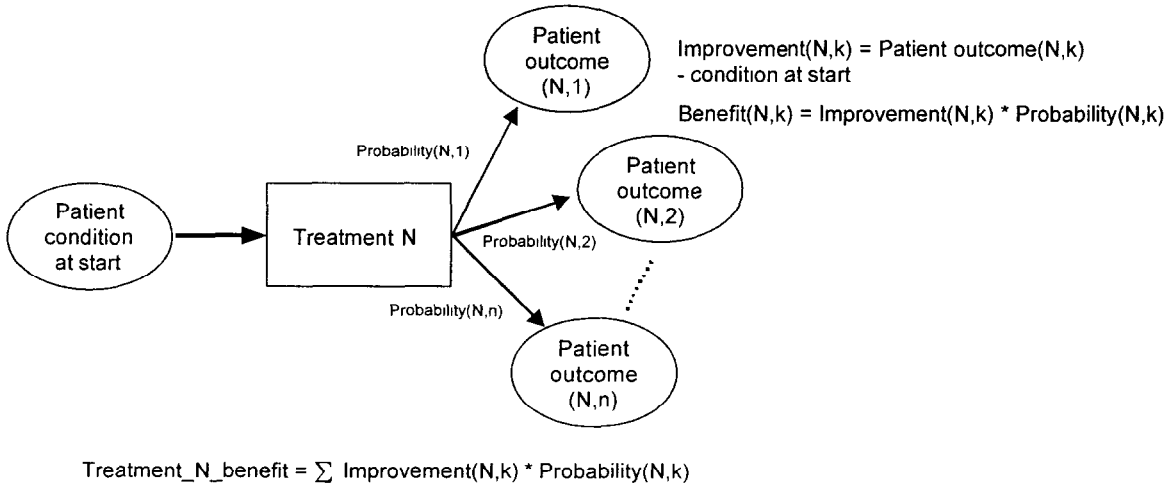



**Figure D.5 — Calculating treatment benefit**

The diagram in Figure D.5 illustrates that for each option (including no treatment) there is likely to be a range of possible outcomes. The improvement is the difference between the patient outcome and the patient condition at the start. Each outcome will have an associated probability. The benefit for each outcome is some function that combines the improvement and the probability of that improvement (e.g. they could be multiplied together). The next stage is to aggregate the benefits from the different outcomes (e.g. they could be summed). The result will be an aggregated benefit for a particular option. The best option is the one with the most positive aggregate benefit.

The following are some of the difficulties that need to be resolved in order to apply this model:

— It will be difficult to compare different outcomes, e.g. which is worse, pain or loss of mobility? Different outcomes can result from the side effects being very different from the initial problem.

— It is difficult to take account of non-stable outcomes. These can arise both from the recovery time and long-term effects.

— It requires detailed knowledge of the numeric values for probabilities. Probability data are often poor, and very important decisions could be made on the basis of poor quality data.

— You need to know the function that combines likelihood and improvement

— This type of approach can only be used in the final comparison of risk and benefit (Clause 7).

#### D.5.2.1 A Simplified Approach

Because of the difficulties in a rigorous approach, it can be expedient to make simplifying assumptions. For example, it will usually prove expedient to consider only the most likely outcomes for each option. Further, one can look for dominant effects and truncate the number of outcomes that are considered.

### D.5.3 Practical Examples Of Risk Benefit Decisions

**Example 1**: Burns can occur where the neutral electrode of a high frequency surgical medical device is attached to the patient. Although conformance to the relevant product standard minimizes the possibility of such burns, they still occur. Nevertheless, this device is indispensable to all kinds of surgical operations; hence, the benefit outweighs the residual risk.

**Example 2**: Although applying x-rays to patients is known to cause harm, the clinical effectiveness of conventional diagnostic imaging almost always justifies its use. However, the unwanted effects of radiation on the patient are not ignored. Standards exist to minimize unnecessary radiation exposure to patients. When a new application of ionizing radiation to diagnostic imaging is contemplated, the manufacturer should demonstrate that the new device achieves a benefit to risk commensurate with what is achieved by existing products that meet current standards.

**Example 3**: X-Ray cancer therapy causes well-known "side effects" such as nausea, lack of appetite, hair loss, etc. The risks of these side effects are accepted because the potential clinical benefit of the treatment outweighs these risks.

**Example 4**: Once implanted, some cochlear implant components such as the implant receiver stimulator with electrode array cannot easily be replaced. They are intended to remain implanted for life (especially in the case of a young adult or child) and must perform reliably for years and even decades. Accelerated reliability testing of these components can be conducted for specific failure mechanisms. However, validating the reliability of components that must last for decades is not practical. Therefore, the overall residual risk including the risk of device failure must be weighed against the benefit afforded by the potential for hearing improvement. Factors to be considered include possible loss of remaining residual hearing during electrode insertion into the cochlea and the risks and benefits of treatment options

## D.6 Overall Residual Risk Evaluation

Overall residual risk evaluation is the point where the manufacturer has to step back, and consider the combined impact of the individual residual risks on the intended use/intended purpose of the device.

Evaluating individual residual risks does not provide assurance that the overall residual risk posed by a device is acceptable. The overall residual risk should be evaluated using the manufacturers risk acceptability criteria established for that purpose. Overall residual risk evaluation needs to be performed by persons with the knowledge, experience, and authority to perform such tasks. It is often desirable to involve application specialists with knowledge of and experience with the device (see 3.3)

Overall residual risk evaluations can be very complicated:

— Risks can originate from many sources, e.g., device design, associated processes including manufacturing, or quality assurance activities. Thus, the need to determine whether overall residual risk is acceptable can require that risks be grouped in some manner to facilitate evaluation, e.g., grouped by hazard, consequence, or some other scheme (manufacturing or installation).

— The individual residual risks can be difficult to combine, e.g., both quantitative and qualitative risk estimates can be present, and, even when only quantitative estimates are used, the uncertainty in risk estimations can vary widely.

There is no standard method for evaluating overall residual risk, and the manufacturer is free to determine the actual method. One approach could be to use independent application specialists to evaluate the acceptability of the system considering aspects such as foreseeable misuse and essential performance. Then, evaluation of the device in the clinical environment could confirm the acceptability

One practical way to evaluate the overall residual risk is to assume that the risks have been allocated into one of the three regions discussed above:

— Broadly acceptable

— ALARP

— Intolerable

At the time that the overall residual risk evaluation is carried out, no individual residual risk should remain in the intolerable region. If a risk remained in this region, the device design would already have been abandoned.

Risks that have been assessed as being broadly acceptable need not be included in the overall residual risk evaluation, provided that the level at which a risk is assessed as being broadly acceptable is not too high. Hence, one need only focus on risks in the ALARP region (see D.3.2).

Risks in the ALARP region will have been reduced to as low as practicable. However, it is possible that the aggregation of all of these risks will cause the overall risk to become intolerable. At this point there are three options:

— The product is abandoned;

— Some method is found for reducing one or more of the individual residual risks; or

— The residual risk is justified on the basis of a risk/benefit analysis. This option should only be taken if there is no practicable way of reducing the risk.

Note that even when the aggregation of risks does not cause the overall risk to become intolerable, the overall risk can be sufficiently high that it is borderline acceptable, and it might be prudent to review the previous decisions on the practicality of reducing individual residual risks.

# Annex E
(informative)

# Risk management plan

The risk management plan is a specific revision controlled document created for each medical device. It can contain completed information or it can reference other documents to fulfil the requirements described in 3.4. The establishment and maintenance of risk management plans can be an element of the manufacturer's quality management system. The risk management plan can be a separate document or it can be integrated within another quality management system document.

Criteria for risk acceptability are derived from the manufacturer's policy for determining acceptable risk. The criteria can be common for similar categories of medical device. Criteria for risk acceptability can be part of the manufacturer's established quality management system, which can be referenced in the risk management plan (see ISO 13485-200X, subclause 7.1).

All elements of the risk management process should be mapped to the manufacturer's defined product life cycle. Some of the elements of the risk management process will occur during the phases of the manufacturer's established product realization process (see ISO 13485:200x) such as the design control. The remaining elements will occur during the other life cycle phases through to product decommissioning. The risk management plan provides this mapping for a specific product either explicitly or by reference to other quality management system documents.

Verifying implementation of risk control measures should occur within an established design control process (see ISO 13485:200x, subclause 7.3). Verifying the effectiveness of risk control measures can require the collection of clinical data, usability studies, etc. The risk management plan will specify how these two distinct verification activities will be carried out. The risk management plan can detail the verification activities explicitly or by reference to the plan for other verification activities.

The risk management plan should identify the personnel with responsibility for the execution of specific risk management activities, for example reviewer(s), expert(s), independent verification specialist(s), individual(s) with approval authority (see 3.2, Management responsibilities). This assignment can be included in a resource allocation matrix defined for the design project.

Review requirements are a generally recognized responsibility of management. The risk management plan should detail how and when these management reviews will occur for a specific device. The requirements for the review of risk management activities could be part of other quality system review requirements (see ISO 13485:200x).

A method of obtaining post-product information can be part of established quality management system procedures (see ISO 13485:200x, subclause 8.2.1). Any manufacturer is supposed to establish generic procedures to collect information from various sources such as users, service personnel, training personnel, incident reports and customer feedback. While a reference to the quality management system procedures can suffice in most cases, product specific requirements should be directly added to the risk management plan.

The requirements identified above can be considered minimum requirements of a risk management plan. Manufacturers can include other items such as time-schedule, risk analysis tools, or a rationale for the choice of specific risk acceptability criteria.

# Annex F
(informative)

# Information on risk analysis techniques

## F.1 General

This annex provides guidance on some available techniques for probabilistic safety analysis that can be used under 4.3. These techniques are complementary and it might be necessary to use more than one of them. The basic principle is that the possible consequences of a postulated event are analyzed step by step.

## F.2 Preliminary Hazard Analysis (PHA)

PHA is an inductive method of analysis whose objective is to identify the hazards, hazardous situations and events that can cause harm for a given activity, facility or system. It is most commonly carried out early in the development of a project when there is little information on design details or operating procedures and can often be a precursor to further studies. It can be useful when analysing existing systems or prioritising hazards where circumstances prevent a more extensive technique from being used.

A PHA formulates a list of hazards and generic hazardous situations by considering characteristics such as:

a) materials used or produced and their reactivity;

b) equipment employed;

c) operating environment;

d) layout;

e) interfaces among system components, etc.

The method is completed with the identification of the possibilities that the accident happens, the qualitative evaluation of the extent of possible injury or damage to health that could result and the identification of possible remedial measures. PHA should be updated during the phases of design, construction and testing to detect any new hazards and make corrections, if necessary. The results obtained can be presented in different ways such as tables and trees.

See IEC 60300-3-9 first edition A.5 for more information on the procedures for preliminary hazard analysis.

## F.3 Failure Mode and Effects Analysis (FMEA)

FMEA is a technique by which the consequences of an individual component fault mode are systematically identified and evaluated. It is an inductive technique using the question "What happens to the output if . . ?" Components are analyzed one at a time, thus generally looking at a single-fault condition. This is done in a "bottom-up" mode, i.e., following the procedure to the next higher functional system level.

The FMEA is not restricted to a failure of a component's design but can also include failures in the manufacturing and assembling of components (Process FMEA) and the use or misuse of the device by the end user (Application FMEA). FMEA can be extended to incorporate an investigation of the degree of severity of the consequences, their respective probabilities of occurrence and their detectability, and can become a so-called Failure Mode Effect and Criticality Analysis (FMECA). In order to perform such an analysis, the construction of the medical device should be known in some detail.

FMEA can also be a useful technique to deal with human error. It can also be used to identify hazards and thus provide valuable input to a Fault Tree Analysis (FTA).

Disadvantages of this technique can arise from difficulties in dealing with redundancies and the incorporation of repair or preventive maintenance actions, as well as its restriction on single-fault conditions.

See IEC 60812 for more information on the procedures for FMEA.

## F.4 Fault Tree Analysis (FTA)

FTA is primarily a means of analyzing hazards identified by other techniques and starts from a postulated undesired consequence, also called a "top event." In a deductive manner, starting with the top event, the possible causes or fault modes of the next lower functional system level causing the undesired consequence are identified. Following stepwise identification of undesirable system operation to successively lower system levels will lead to the desired system level, which is usually the component fault mode. This will reveal the sequences most likely to lead to the postulated consequence. It has therefore proved to be useful for forensic purposes.

The results are represented pictorially in the form of a tree of fault modes. At each level in the tree, combinations of fault modes are described with logical operators (AND, OR, etc.). The fault modes identified in the tree can be events that are associated with hardware faults, human errors, or any other pertinent event which leads to the undesired event. They are not limited to the single-fault condition.

FTA allows a systematic approach which, at the same time, is sufficiently flexible to allow analysis of a variety of factors, including human interactions. FTA is primarily used in risk analysis as a tool to provide an estimate of fault probabilities. The pictorial representation leads to an easy understanding of the system behavior and the factors included, but, as the trees become large, processing of fault trees can require computer systems.

See IEC 61025 for more information on the procedures for FTA.

## F.5 Hazard and Operability Study (HAZOP)

HAZOP is similar to an FMEA. HAZOP is based on a theory that assumes accidents are caused by deviations from the design or operating intentions. It is a systematic technique for identifying hazards and operability problems. It was originally developed for use in the chemical process industry. While the use of HAZOP studies in the chemical industry focuses on deviations from design intent, there are alternative applications for a medical device developer. A HAZOP can be applied to the operation/function of the medical device (e.g., to the existing methods/processes used for the diagnosis, treatment, or alleviation of disease as the "design intent"), or to a process used in the manufacture or maintenance/service of the medical device (e.g., sterilization) that can have significant impact on the function of the medical device. Two particular features of a HAZOP are as follows:

a) it uses a team of people with expertise covering the design of the medical device and its application; and

b) guide words (NONE, PART OF, etc.) are used to help identify deviations from normal use.

The objectives of the technique are:

— to produce a full description of the medical device and how it is intended to be used;

— to review systematically every part of the intended use/intended purpose to discover how deviations from the normal operating conditions and the intended design can occur; and

— to identify the consequences of such deviations and to decide whether these consequences can lead to hazards or operability problems.

When applied to the processes used to manufacture a medical device, the last objective is particularly useful in those cases where the medical device characteristics depend upon the manufacturing process.

See IEC 61882 for more information on the procedures for HAZOP.

## F.6 Hazard Analysis and Critical Control Point (HACCP)

Hazard Analysis and Critical Control Point (**HACCP**) system is a form of hazard analysis. It was originally developed by NASA to assure freedom of food poisoning of astronaut. HACCP could be applied in many other situations. It is a systematic, proactive, and preventive method system for assuring product quality, reliability, and safety. It is based on a common-sense structured approach applying technical and scientific principles to analyze, evaluate, prevent, and control the risk or the adverse consequence(s) of hazard(s) due to the design, development, production, and use of products. An effective HACCP system when properly applied and implemented can minimize regulatory inspection time, improve product reliability and safety, and reduce cost of poor quality.

The core curriculum of HACCP consists of the following seven principles (the inserted references to this standard is intended for reference only):

1. Conduct hazard analysis (4.3) and identify preventive measures (6.2)
2. Determine the critical control points (CCPs) (6.2)
3. Establish critical limits (4.2 and 5)
4. Monitor each CCP (6.3 and 9)
5. Establish corrective actions (Clause 9)
6. Establish verification procedures (6.3 and 9)
7. Establish record-keeping and documentation procedures (3.5 and 8)

Each product has its own hazards that are related to its life cycle, such as hazards related to design, development, production, and use. The following is a list of some typical hazards that should be analyzed, evaluated, and prevented **(HACCP Principle 1)**.

- Physical
- Chemical
- Radiation
- Performance quality
- Delayed treatment
- Biological
- Electrical
- Explosion
- Misdiagnosis
- Use errors

The heart of an effective HACCP system focuses on the continuing control and monitoring **(HACCP Principles 2, 3, & 4)**, of the identified hazards. A manufacturer demonstrates the effectiveness of

established control measure(s), **(HACCP Principles 5 & 6)**, by establishing methodically documented process mapping, process hazard analysis, and critical control plan, **(HACCP Principle 7)**.

The HACCP system uses the following tools as documented evidence for record keeping:

**Process Flow Diagram**

The purpose of the diagram is to provide a clear and simple description of the steps involved in the process. The diagram is necessary to the HACCP team in its subsequent work. The diagram can also serve as a future guide for others who must understand the process for their verification activities. The scope of the flow diagram must cover all the processing steps that are directly under the control of the manufacturer.

**Hazard Analysis Worksheet**

Hazard analysis is the identification of hazards and of their initiating causes. The analysis records contain: 1] the identification and listing of steps in the process where actual and potential hazards of significance occur; 2] the listing of all identified hazards and their significance associated with each step; 3] the listing of all preventive measures to control each hazard; 4] the identification of all the CCPs and their monitoring and controls.

**HACCP Plan**

The written document which is based upon the seven principles of HACCP and which delineates the procedures to be followed to assure the control of a specific design, product, process or procedure. The plan includes: 1] all critical control points and critical limits identification; 2] monitoring and continuing control activities; 3] corrective action, verification, and record-keeping activities.

For details, refer to US Food and Drug Administration's Medical Device Risk Management Training Using HACCP Principles, 1st Edition, April 2000.

## F.7 Potential Application of the Above Techniques

Table F.1 lists examples of risk analysis techniques that could be applied in the risk management process:

**Table F.1 — Examples of risk analysis techniques**

| Clause | PHA | FTA | FME(C)A (Design/ component | FME(C)A (Process) | FME(C)A (Application system) | HAZOP | HACCP |
|---|---|---|---|---|---|---|---|
| 4.1 Risk Analysis procedure | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| 4.2 Intended use/ID characteristics | ✓ | ✓ | | | | ✓ | ✓ |
| 4.3 ID of known or foreseeable hazards | ✓ | ✓ | | | | ✓ | ✓ |
| 4.4 Estimation of the risk(s) for each hazard | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| 5~9 Risk Evaluation ~ Post-Production Information | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| NOTE There are other recognised risks analyses techniques available, such as those listed in IEC 60300-3-9 | | | | | | | |

# Annex G
(informative)

# Questions that can be used to identify medical device characteristics that could impact on safety

## G.1 General

Subclause 4.2 requires that the manufacturer identifies those characteristics of the medical device that could affect safety. Consideration of these characteristics is an essential step in identifying the hazards of the medical device as required in 4.3 because under certain conditions those characteristics can result in hazards being generated. One way of doing this is to ask a series of questions concerning the manufacture, use, and ultimate disposal of the medical device. If one asks these questions from the point of view of all the individuals involved (e.g., users, maintainers, patients, etc.), a more complete picture can emerge of where the potential hazards can be found. The following questions can aid the reader in identifying all the characteristics of the medical device that could affect safety.

The list is not exhaustive, or representative of all devices, and the reader is cautioned to add questions that can have applicability to the particular medical device

## G.2 Questions

### G.2.1 What is the intended use/intended purpose and how is the medical device to be used?

Factors that should be considered include:

What role is the medical device intended to play in:

— the diagnosis, prevention, monitoring, treatment or alleviation of disease;

— compensation for injury or handicap; or

— replacement or modification of anatomy, or control of conception?

Is the medical device life sustaining or life supporting?

Is special intervention necessary in the case of failure of the medical device?

Are there special concerns about interface design features that could contribute to inadvertent use error (see A.2.27)?

### G.2.2 Is the medical device intended to contact the patient or other persons?

Factors that should be considered include the nature of the intended contact, i.e., surface contact, invasive contact, and/or implantation and, for each, the period and frequency of contact.

### G.2.3 What materials and/or components are incorporated in the medical device or are used with, or are in contact with, the medical device?

Factors that should be considered include whether characteristics relevant to safety are known.

### G.2.4 Is energy delivered to and/or extracted from the patient?

Factors that should be considered include the type of energy transferred and its control, quality, quantity, and duration.

### G.2.5 Are substances delivered to and/or extracted from the patient?

Factors that should be considered include whether the substance is delivered or extracted, whether it is a single substance or range of substances, the maximum and minimum transfer rates, and control thereof.

### G.2.6 Are biological materials processed by the medical device for subsequent re-use?

Factors that should be considered include the type of process and substance(s) processed (e.g., auto-transfusion, dialysis).

### G.2.7 Is the medical device supplied sterile or intended to be sterilized by the user, or are other microbiological controls applicable?

Factors that should be considered include whether the medical device is intended for single-use or to be re-usable, and also any packaging, the shelf-life, and any limitation on the number of re-use cycles or type of sterilization process to be used.

### G.2.8 Is the medical device intended to be routinely cleaned and disinfected by the user?

Factors that should be considered include the types of cleaning or disinfecting agents to be used and any limitations on the number of cleaning cycles. In addition, the design of the medical device can influence the effectiveness of routine cleaning and disinfection.

### G.2.9 Is the medical device intended to modify the patient environment?

Factors that should be considered include temperature, humidity, atmospheric gas composition, pressure, and light.

### G.2.10 Are measurements taken?

Factors that should be considered include the variables measured and the accuracy and the precision of the measurement results.

### G.2.11 Is the medical device interpretative?

Factors that should be considered include whether conclusions are presented by the medical device from input or acquired data, the algorithms used, and confidence limits.

### G.2.12 Is the medical device intended for use in conjunction with medicines or other medical technologies?

Factors that should be considered include identifying any medicines or other medical technologies that can be involved and the potential problems associated with such interactions, as well as patient compliance with the therapy.

### G.2.13 Are there unwanted outputs of energy or substances?

Energy-related factors that should be considered include noise and vibration, heat, radiation (including ionizing, non-ionizing, and ultraviolet/visible/infrared radiation), contact temperatures, leakage currents, and electric and/or magnetic fields.

Substance-related factors that should be considered include substances used in manufacturing, cleaning or testing having unwanted physiological effects if they remain in the product.

Other substance-related factors that should be considered include discharge of chemicals, waste products, and body fluids.

### G.2.14 Is the medical device susceptible to environmental influences?

Factors that should be considered include the operational, transport, and storage environments. These include light, temperature, vibrations, spillage, susceptibility to variations in power and cooling supplies, and electromagnetic interference.

### G.2.15 Does the medical device influence the environment?

Factors that should be considered include the effects on power and cooling supplies, emission of toxic materials, and the generation of electromagnetic interference.

### G.2.16 Are there essential consumables or accessories associated with the medical device?

Factors that should be considered include specifications for such consumables or accessories and any restrictions placed upon users in their selection of these.

### G.2.17 Is maintenance and/or calibration necessary?

Factors that should be considered include whether maintenance and/or calibration are to be carried out by the operator or user or by a specialist. Are special substances or equipment necessary for proper maintenance and/or calibration?

### G.2.18 Does the medical device contain software?

Factors that should be considered include whether software is intended to be installed, verified, modified, or exchanged by the user and/or operator.

### G.2.19 Does the medical device have a restricted shelf-life?

Factors that should be considered include labelling or indicators and the disposal of such medical devices.

### G.2.20 Are there any delayed and/or long-term use effects?

Factors that should be considered include ergonomic and cumulative effects. Examples could include pumps for saline that corrode over time, mechanical fatigue, loosening of straps and attachments, vibration effects, labels wear or fall off, long term material degradation.

### G.2.21 To what mechanical forces will the medical device be subjected?

Factors that should be considered include whether the forces to which the medical device will be subjected are under the control of the user or controlled by interaction with other persons.

### G.2.22 What determines the lifetime of the medical device?

Factors that should be considered include aging and battery depletion.

### G.2.23 Is the medical device intended for single use?

### G.2.24 Is safe decommissioning or disposal of the medical device necessary?

Factors that should be considered include the waste products that are generated during the disposal of the medical device itself. For example, does it contain toxic or hazardous material, or is the material recyclable?

### G.2.25 Does installation or use of the medical device require special training or special skills?

### G.2.26 How will information for safe use be provided?

Factors that should be considered include:

— whether information will be provided directly to the end user by the manufacturer or will it involve the participation of third parties such as installers, care providers, health care professionals, pharmacists and whether this will this have implications for training

— commissioning and handing over to the end user and whether it is likely/possible that installation can be carried out by people without the necessary skills.

### G.2.27 Will new manufacturing processes need to be established or introduced?

Factors that should be considered include new technology or a new scale of production.

### G.2.28 Is successful application of the medical device critically dependent on human factors such as the user interface?

Factors that should be considered are user interface design features that can contribute to use error. Features should be designed so that they cannot be easily misused by busy users in an environment where distractions are commonplace, e.g., device control, symbols used, ergonomic features, physical design and layout, hierarchy of operation, menus for software driven devices, visibility of warnings, audibility of alarms, standardized colour coding. These considerations include, but are not limited to, the following.

#### G.2.28.1 Does the medical device have connecting parts or accessories?

Factors that should be considered include the possibility of wrong connections, differentiation, similarity to other products' connections, connection force, feedback on connection integrity, and over- and under-tightening.

#### G.2.28.2 Does the medical device have a control interface?

Factors that should be considered include spacing, coding, grouping, mapping, modes of feedback, blunders, slips, control differentiation, visibility, direction of activation or change, whether the controls are continuous or discrete, and the reversibility of settings or actions.

#### G.2.28.3 Does the medical device display information?

Factors that should be considered include visibility in various environments, orientation, populations and perspectives, clarity of the presented information, units, colour coding, and the accessibility of critical information.

#### G.2.28.4 Is the medical device controlled by a menu?

Factors that should be considered include complexity and number of layers, awareness of state, location of settings, navigation method, number of steps per action, sequence clarity and memorization problems, and importance of control function relative to its accessibility.

#### G.2.28.5 Is there a possibility of deliberate misuse?

Factors that should be considered are incorrect use of connectors, disabling safety features or alarms, neglect of manufacturers recommended maintenance.

#### G.2.28.6 Will the device be used by persons with special needs?

Factors that should be considered include the intended user, the mental and physical abilities, skill, and training of the user, ergonomic aspects, the environment in which it is to be used, by whom it will be installed, and whether the patient can control or influence the use of the medical device. Special attention should be paid to intended users with special needs such as handicapped persons, the elderly, and children. Their special needs might include assistance by another person to enable the use of a medical device. Is the medical device intended to be used by individuals with various skill levels and cultural backgrounds?

### G.2.29 Is the medical device intended to be mobile or portable?

Factors that should be considered are the necessary grips, handles, wheels, brakes, mechanical stability, and durability.

### G.2.30 Does the use of the device depend on essential performance requirements?

Factors that should be considered include whether the absence of essential performance would result in an unacceptable risk. Examples are:

— Accuracy of a life-supporting function or correct administration of a drug by a syringe pump where inaccuracy/incorrect administration would cause an unacceptable risk of harm to the patient;

— The ability of an electrocardiograph/monitor to recover from the effects of the discharge of a defibrillator where the failure to recover could lead to an incorrect response by the medical staff that would present an unacceptable risk of harm to the patient;

— Correct operation of an alarm in an intensive care or operating room monitoring system where an incorrect/missing alarm could lead to an incorrect response by the medical staff that would present an unacceptable risk of harm to the patient

— Correct diagnostic information from medical electrical equipment that is likely to be relied upon to determine treatment, where incorrect information could lead to an inapproprate treatment that would present an unacceptable risk of harm to the patient;

An additional example of essential performance is performance of medical electrical equipment required for a procedure associated with a known risk to the patient, where a failure of the medical electrical equipment to perform correctly would necessitate a repetition of this procedure thus invalidating the original risk/benefit assessment."

# Annex H
(informative)

# Guidance on risk analysis for *in vitro* diagnostic medical devices

## H.1 General

This annex provides additional guidance on the risk analysis of *in vitro* diagnostic medical devices, taking into account the particularities and specific aspects of these medical devices. The use of *in vitro* diagnostic medical devices does not create any direct risk to the patient or the person subjected to the examination, as they are not applied in or on the human body. Under certain circumstances, however, indirect risks can result from hazards associated with *in vitro* diagnostic medical devices, leading or contributing to erroneous decisions. In addition, use-related hazards and their associated risks should be considered.

## H.2 Identification of hazards

In addition to those aspects mentioned in Annex J, the following aspects should be considered in identifying potential hazards for the patient or the person subjected to examination:

— batch inhomogeneity, batch-to-batch inconsistency;

— common interfering factors;

— carry-over effects;

— specimen identification errors;

— stability problems (in storage, in shipping, in use, after first opening of the container);

— problems related to taking, preparation, and stability of specimens;

— inadequate specification of prerequisites;

— inadequate test characteristics.

Potential hazards for the user can arise from radioactive, infectious, toxic, or otherwise hazardous ingredients of reagents and from the packaging design. For instruments, the problem of potential contamination during handling, operation, and maintenance should be considered in addition to the non-specific instrument-related hazards (e.g., energy hazards).

## H.3 Risk estimation

In estimating the risk for each hazard, the following aspects should be taken into account:

— extent of reliance on the analytical result (contribution to the medical decision);

— plausibility checks;

— availability and use of controls;

— quality assurance measures/techniques applied in medical laboratories;

— detectability of deficiencies/errors;

— situations of use (e.g., emergency cases);

— professional use/non-professional use;

— method of presentation of information.

# Annex I
(informative)

# Guidance on risk analysis process for toxicological hazards

## I.1 General

This annex provides guidance on the application of risk analysis, with respect to toxicological hazards. Toxicological hazards are due to chemical constituents causing biological harm. ISO 10993-1 sets out the general principles for the biological evaluation of materials/medical devices.

Efforts should be made to avoid unnecessary testing using animals. Attention is drawn to ISO 10993-2 on animal welfare requirements, and to relevant national or regional regulations, which can indicate that tests should be omitted if the omission can be scientifically justified.

## I.2 Estimation of toxicological risks

### I.2.1 Factors to be taken into account

The toxicological risk analysis should take account of

— the chemical nature of the materials,

— prior use of the materials, and

— biological safety test data.

The amount of data required and the depth of the investigation will vary with the intended use/intended purpose and are dependent upon the nature and duration of patient contact. Data requirements are usually less stringent for packaging materials, medical devices contacting intact skin, and any component of a medical device that does not come into direct contact with body tissues, infusible liquids, mucous membranes, or compromised skin.

Current knowledge of the material/medical device provided by scientific literature, previous clinical experience, and other relevant data should be reviewed to establish any need for additional data. In some cases, it can become necessary to obtain formulation data, residue data (e.g., from sterilization processes, monomers), biological test data, etc.

### I.2.2 Chemical nature of the materials

Information characterizing the chemical identity and biological response of materials is useful in assessing a medical device for its intended use/intended purpose. Some factors that can affect the biocompatibility of the material include:

— the identity, concentration, availability, and toxicity of all constituents (e.g., additives, processing aids, monomers, catalysts, reaction products), and

— the influence of biodegradation and corrosion on the material.

Where reactive or hazardous ingredients have been used in, or can be formed by, the production, processing, storage or degradation of a material, the possibility of exposure to residues should be

considered. Information on residue concentration and/or leaching can be necessary. This can take the form of experimental data or information on the chemistry of the materials involved.

Where the necessary data (e.g., complete formulation data) are not available to a manufacturer because of confidentiality, verification should be obtained that an assessment has been carried out of the suitability of the material for use in the proposed application.

### I.2.3 Prior use

Available information on previous uses of each material or intended additive and on any adverse reactions encountered should be reviewed. However, the previous use of an ingredient or material does not necessarily assure its suitability in similar applications. Account should be taken of the intended use/intended purpose, the concentration of the ingredients, and current toxicological information.

### I.2.4 Biological safety test data

ISO 10993-1 gives guidance on which tests in the ISO 10993 series should be considered for a particular application. The need for testing should be reviewed on a case-by-case basis in the light of existing data, so that unnecessary testing is avoided.

# Annex J
(informative)

# Examples of hazards and contributing factors that can initiate foreseeable sequences of events that can result in hazardous situations

## J.1 General

Subclause 4.3 requires that the manufacturer compile a list of hazards and foreseeable sequence of events that can result in a hazardous situation. This annex provides a non-exhaustive list of possible hazards, which can be associated with different medical devices, together with contributing factors that can initiate foreseeable sequences of events that can result in hazardous situations, which can result in harm. Contributing factors are often the trigger of the sequence of events that can lead to harm. This annex explains the relationship between the different aspects of contributing factors, hazards and harm in order to help the manufacturer to foresee possible sequences of events. To recognize a consistent sequence from hazards to hazardous situations that can result in harm is critical for estimating the probability of occurrence and severity of harm that could result from identified hazards.

## J.2 Examples of hazards

The list in Table J.1 can be used to aid in the identification of hazards associated with a particular medical device and contributing factors.

**Table J.1 — Examples of hazards**

| Examples of energy hazards | Examples of biological and chemical hazards | Examples of hazards to environment and property | Examples of hazards related to information |
|---|---|---|---|
| **Electromagnetic energy**<br>— Line voltage<br>— Leakage current<br>  — Enclosure leakage current<br>  — Earth leakage current<br>  — Patient leakage current<br>— Electric fields<br>— Magnetic fields<br>**Radiation energy**<br>— Ionizing radiation<br>— Non-ionizing radiation<br>**Thermal energy**<br>— High temperature<br>— Low temperature | — bio-contamination<br>  — by bacteria or<br>  — viruses or<br>  — inability to maintain hygienic safety,<br>— contact with organic material skin (or airway),<br>— contact with organic material invasive,<br>— contact with non-organic material (skin /airway /invasive), | — medical gases,<br>— anaesthetic agents,<br>— emission of electromagnetic fields,<br>— substances that produce adverse physiological effects, e.g. trace materials, cleaning, disinfection or testing agents. | — inadequate labeling,<br>— inadequate operating instructions, such as<br>  — inadequate specification of accessories to be used with the medical device (examples),<br>  — inadequate specification of pre-use checks (examples),<br>  — over-complicated operating instructions (examples), |

Table J.1 — Examples of hazards

| Examples of energy hazards | Examples of biological and chemical hazards | Examples of hazards to environment and property | Examples of hazards related to information |
|---|---|---|---|
| **Mechanical energy**<br>— Gravity<br>— Falling<br>— Suspended masses<br>— Vibration<br>— Release of stored energy<br>— Moving parts<br>— Squeezing<br>— Crushing<br>— Shearing<br>— Cutting or severing<br>— Entanglement<br>— Trapping<br>— Stabbing or puncturing<br>— Friction or abrasion<br>— Expelled parts<br>— Instability<br>— Impact<br>— Moving and positioning of patient<br>— Acoustic energy<br>— Ultrasonic energy<br>— Infrasound energy<br>— Sound<br>— High pressure fluid injection, due to leakage | — bio-incompatibility:<br>— toxicity (harm related),<br>— allergenicity (harm related),<br>— mutagenicity (harm related),<br>— oncogenicity (harm related),<br>— teratogenicity (harm related),<br>— carcinogenicity (harm related),<br>— re- and/or cross-infection (harm related),<br>— pyrogenicity (harm related),<br>— substances that produce adverse physiological effects, e.g. trace materials, cleaning, disinfection or testing agents."<br>— Chemical hazards<br>— contact to acids or alkalis | | — inadequate specification of service and maintenance (examples),<br>— insufficient warning of side effects,<br>— inadequate warning of hazards likely with re-use of single-use medical devices,<br>— incorrect measurement and other metrological aspects. |

## J.3 Examples of contributing factors

Contributing factors can, for example, come from:

— Design:
  — Material degradation (e.g. ageing),
  — Incompatibility with other devices with which the device is intended to be used;

— Manufacturing processes:
  — Change of manufacturing processes,
  — Insufficient material compatibility information,
  — Insufficient control of manufacturing processes,
  — Insufficient control of subcontractors;

- Transport and storage:
  - Inadequate packaging (contamination and/or deterioration of the medical device);
- Environmental effects:
  - Corrosion,
  - Degradation,
  - Biodegradation,
  - Electromagnetic fields,
  - Susceptibility to electromagnetic interference;
- Installation, Maintenance and Service;
- Cleaning, disinfection and sterilization;
- Disposal and scrapping;
- Normal Operation:
  - Ageing
  - Inadequate supply of power,
  - Inadequate supply of coolant;
- Use errors:
  - Use by unskilled/untrained personnel,
  - Reasonably foreseeable misuse,
  - Potential for intentional misuse,
  - Confusing or missing instructions for use,
  - Insufficient warning of side effects,
  - Inadequate warning of hazards associated with re-use of single-use medical devices,
  - Incorrect measurement and other metrological aspects,
  - Incompatibility with consumables/accessories/other medical devices,
  - Incorrect formulation,
  - Inability to maintain hygienic safety,
  - Operation outside prescribed environmental conditions (e.g. heat, pressure, time, presence of contamination),
  - Human factors, e.g.:
    - mistakes and judgment errors,
    - lapses and cognitive recall errors,
    - slips and blunders (mental or physical),
    - violation or abbreviation of instructions, procedures, etc.,
    - complex or confusing control system,
    - ambiguous or unclear device state,
    - ambiguous or unclear presentation of settings, measurements, or other information,
    - misrepresentation of results,
    - insufficient visibility, audibility, or tactility,
    - poor mapping of controls to action, or of displayed information to actual state,
    - controversial modes or mappings as compared to existing equipment;

- Failure modes:
  - Erroneous data transfer,
  - Lack of, or inadequate specification for, maintenance including inadequate specification of post- maintenance functional checks,
  - Inadequate maintenance,
  - Lack of adequate determination of the end of life of the medical device,
  - Loss of electrical/mechanical integrity,
  - Deterioration in function (e.g., gradual occlusion of fluid/gas path, or change in resistance to flow, electrical conductivity) as a result of repeated use,
  - Failure to perform to essential performance requirements.

## J.4 Examples for relations between identified hazards, hazardous situations, contributing factors and harms

Table J.2 illustrates the relationship between hazards, harm, hazardous situations and contributing factors. The order of the columns has been chosen to illustrate the typical thought process rather than the logical connection between the elements in the columns.

**Table J.2 — Relationship between hazards, harm, hazardous situations and contributing factors**

| Hazard | Potential harm | Hazardous situation | Contributing factor |
|---|---|---|---|
| Line voltage | Heavy burns, heart fibrillation, death | Line voltage directly applied to patient through electrodes | Electrodes are unintentionally plugged into line cable plug, instead of the electrode cable block |
| Excessive high frequency currents | Burns | Excessive high-frequency currents during electro-surgery on wrong path through the patient/user | Return electrode plate disconnected, other connectors have contact with the patient through which currents flow. |
| Excessive leakage current | Fibrillation, death | Grounding of interconnected electrical system component not appropriately installed | People exposed to excessive enclosure leakage current |
| Inflated arm cuff | Necrosis, thrombosis, loss of arm | Failure of software controlling cuff pressure or<br>Failure of valve to release pressurized air from the cuff | Non-invasive blood pressure cuff inflated too long time above systolic pressure levels |
| Moving objects made of magnetic material | Wound, fracture, death | Failure to remove any object made of magnetic material before the start of the MRI procedure | People in MRI exposed to moving objects made of magnetic material, e.g. a bottle for anesthetic gas |
| High temperature | Skin burn | Design or verification/validation not adequate | $SpO_2$ sensor LED becomes to hot |
| Microbial contamination | Bacterial infection, death | Reuse of tubing without disinfection prior to use or<br>Failure of a bacterial filter | Bacteria released into airway of a patient during anesthesia. |
| Irritating disinfectant | Skin reddening, minor burns | Insufficient cleaning instructions for surfaces that can get in contact with patients | Patient skin exposed to irritating disinfectant |

**Table J.2 — Relationship between hazards, harm, hazardous situations and contributing factors**

| Hazard | Potential harm | Hazardous situation | Contributing factor |
|---|---|---|---|
| Excessive volume of gas in the blood | Gas embolism, brain damage, death | Hazardous solvents, residual from the manufacturing process, released into the blood | Development of gas in the blood during dialysis |
| Oxygen delivery | Retinal detachment, blindness | Misinterpretation or incorrect indication of the measured oxygen levels on oxygen monitor | Excessive volumes of oxygen delivered to a premature newborn |
| Parts made of latex | Skin irritation, allergic shock, death | Improper material used | Device containing latex applied to patient being allergic to latex |

# Annex K
(informative)

# Communication of information on residual risk

## K.1 Introduction

Because communication of information on residual risk is an essential, but often neglected, part of the overall risk management process, it is desirable that a risk communication policy be developed.

In 6.2 c), a manufacturer may need to communicate risk as a risk control measure, and in 6.4, the manufacturer must decide which information on residual risk to put into the accompanying documents.

The purpose of this annex is to provide further guidance on how information on residual risk can be communicated effectively and in such a way that risk awareness is promoted in the best possible way throughout the life cycle of the medical device.

### K.1.1 Risk communication in the healthcare environment

In order to better understand how to improve risk communication, users of this standard should first identify those key stakeholders to whom risk information should be communicated. These could include, but are not limited to:

— medical professionals

— other workers involved in the healthcare environment

— regulatory bodies

— Notified Bodies or Conformity Assessment Bodies

— patients and patients' associations

— pressure groups

— healthcare insurance providers

In each of these cases:

— the way in which information is communicated,

— the level of information provided,

— the language used in communication, and

— the clarity and understandability of the information provided

are all key elements to consider. Some factors that can be useful in addressing the risk communication needs of some of these stakeholders will be examined in more detail in K.1.3.

### K.1.2 Why communicate risk?

First of all, communicating residual risk can be the result of the risk control process. In addition, there could be legal requirements to communicate residual risk in many regulatory systems. There is also an ethical and moral imperative to maximize the level of safety for patients, professional users, other associated healthcare personnel, third parties and the environment. In many countries and regions, there is legislation that covers the protection of workers in the workplace and employers are often obliged to provide safe working practices and procedures.

It should be remembered also that, although this standard principally addresses risks associated with medical devices in relation to their being placed on the market, the principles of risk management are applicable to the whole life cycle of the device.

In principle, this means that healthcare workers and others are also key stakeholders in relation to the safe use of medical devices in the healthcare environment and are important members of the "risk management chain". The provision of information that will facilitate safe use and disposal of devices is therefore a key element of risk management.

### K.1.3 Some questions that can be useful in developing an effective risk communication policy

#### K.1.3.1 Some particular issues to consider in formulating risk communication information

This is a key question and very much depends upon the nature of the risks involved. In many cases the use of "traditional" labeling and symbols (often as provided for by legislation) are appropriate. However, it should be considered whether the use of such labeling and symbols is sufficient in itself. Factors to consider include the following:

— Is the information going to reach some of the key stakeholders?

An example of this could be information provided with medical devices incorporating sharps. There will normally be warnings and information provided with the instructions for use, and commonly on the sterile barrier system in the case of a single use sterile device. These can include warnings or cautions such as "Dispose of in a sharps container" or "This product contains natural rubber latex which may cause allergic reactions".

After use, however, such protective barrier systems or packaging are normally discarded by the professional healthcare worker. There is, therefore, need to install a "safety culture" that will become second nature to avoid the risk of sharps injuries or allergic reactions to other downstream workers, e.g. those responsible for the safe disposal of such devices.

— Is there a need for training?

Risks of injury are particularly prevalent with new medical professional staff or with those that are unfamiliar with the correct intended use of the device. Training by the manufacturer would be necessary in such cases.

Should professional training, e.g. in medical or nursing school, be reinforced by information provided by industry that addresses some of the most common risks?

— Is there a risk of complacency?

With procedures that are performed many times on a daily basis, there is always the risk that bad habits or complacency may set in. Factors that could be considered include:

— Is there a need for "refresher training"?

Is there a need for aids such as posters or other items that remain visible in the workplace that reinforce good practice?

— Are healthcare and other professional workers aware of the risks and of the consequences of injury or harm?

There is ample evidence to demonstrate, for example, that many healthcare workers remain unvaccinated against infectious agents such as Hepatitis B, despite the high prevalence of such infectious agents in the healthcare facility environment. Once again, an active approach towards encouraging proactive and commonsense measures can be appropriate.

— Are there others involved, e.g. patients and carers, who do not necessarily understand the nature of the risk and of possible consequences?

It is particularly important to consider risk communication carefully when a device will be used directly by the patient or a carer, not necessarily under direct medical supervision.

Such users do not necessarily understand technical language nor view the concept of "risk" in the same way as the manufacturer. There is, therefore, a particular need for clarity in risk communication aimed at such target groups.

— Is there a need for research to characterize better the understanding of risk amongst different target groups?

This indeed can be a very useful and necessary step in formulating an effective risk communion message.

### K.1.3.2 How important are the means/media used in risk communication?

As mentioned already in K.1.3.1, this can depend very much on the nature of the risk and on the intended target group. In some cases, "traditional" labeling/information provided with the device can be adequate. Attention is drawn to the fact that, for home users, standards have already been prepared in some healthcare domains, e.g. in-vitro diagnostics, to ensure an effective approach to the correct use of the device in question and to risk communication. In other cases, however, it may be prudent to consider a more "proactive" approach to risk communication. There are numerous channels in which risk information can be communicated and these include, amongst others:

— Professional publications

— Educational programmes

— In-service training and "refresher" programmes, provided by professionals, manufacturers, independent experts or a combination of these

— Conference, workshops or seminars aimed at raising risk awareness amongst particular target groups

— Audiovisual aids, e.g. videos, posters, etc.

— Workplace "reminders", e.g. messages on work equipment such a mouse mats, pens, giveaways

— Dedicated internet sites

NOTE While they can be a means of providing a great deal of risk information, a disadvantage of internet sites is that the professional or other target user has to actively seek the required information.

# Bibliography


[1] ISO/IEC Guide 2:1996, *Standardization and related activities—General vocabulary.*

[2] ISO/IEC Guide 51:1999, *Safety aspects—Guidelines for the inclusion in standards.*

[3] ISO 9000-3:1991, *Quality management and quality assurance standards—Part 3: Guidelines for the application of ISO 9001 to the development, supply and maintenance of software.*

[4] ISO 9001:2000, *Quality management systems—Requirements.*

[5] ISO 10993-1, *Biological evaluation of medical devices—Part 1: Evaluation and testing.*

[6] ISO 10993-2, *Biological evaluation of medical devices—Part 2: Animal welfare requirements.*

[7] ISO 10993-17, *Biological evaluation of medical devices—Part 17: Establishment of allowable limits for leachable substances using health-based risk assessment.*

[8] ISO 13485:200x, *Medical devices—Quality management systems—System requirements for regulatory purposes.*

[9] ISO 14969, *Quality management systems—Medical devices—Guidance on the application of ISO 13485 and ISO 13488.*

[10] ISO 15189, *Quality management in the medical laboratory.*

[11] IEC 60300-3-9, *Dependability management—Part 3: Application guide—Section 9: Risk analysis of technological systems.*

[12] IEC/TR 60513, *Fundamental aspects of safety standards for medical electrical equipment.*

[13] IEC 60601-1:1988, *Medical electrical equipment—Part 1: General requirements for safety.*

[14] IEC 60601-1-4, *Medical electrical equipment—Part 1: General requirements for safety—4: Collateral standard: Programmable electrical medical systems.*

[15] IEC 60812, *Analysis techniques for system reliability—Procedures for failure mode and effects analysis (FMEA).*

[16] IEC 61025, *Fault tree analysis (FTA).*

[17] IEC 61882, *Guide for hazard and operability studies (HAZOP studies).*

[18] EN 12442-1, *Animal tissues and their derivatives utilized in the manufacture of medical devices—Part 1: Analysis and management of risk.*

[19] 90/285/EEC, Council Directive of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices (90/385/EEC) as amended by Council Directive 93/42/EEC of 14 June 1993 concerning medical devices and Council Directive 93/68/EEC of 22 July 1993.

[20] 93/42/EEC, Council Directive 93/42/EEC of 14 June 1993 concerning medical devices as amended by Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices.

[21] 98/79/EC, Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices.

[22] The *Codex Alimentarius* Commission and the FAO/WHO Food Standards Programme: Complete Texts. E-mail codex@fao.org.

[23] Medical Device HACCP Training Curriculum, York, PA: Association of Food and Drug Officials, April 2000. To buy curriculum: http://www.afdo.org/meddevicehaccp.asp.

[24] Hazard Analysis and Critical Control Points Principles and Application Guidelines, Adopted, August 14, 1997 National Advisory Committee on Microbiological Criteria for Foods http://vm.cfsan.fda.gov/~comm/nacmcfp.html.