INTERNATIONAL STANDARD

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Medical devices — Application of risk management to medical devices

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

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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.ch
Web www.iso.ch

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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 3.

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 International Standard 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.*

Requirements concerning the risk analysis component of the risk management process were developed first and published as ISO 14971-1:1998, with the intention that the requirements for risk evaluation, risk control and post-production information evaluation could be covered in additional part(s), but all the requirements have now been incorporated into this International Standard.

This first edition of ISO 14971 cancels and replaces ISO 14971-1:1998.

For purposes of future IEC maintenance, Subcommittee 62A has decided that this publication remains valid until 2004. 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 G 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 judgement are applied systematically to manage these risks.

As a general concept, activities in which an individual, organization or government is involved can expose those or other stakeholders to hazards which may 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 the occurrence of harm, that is, how often the harm may 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 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 may 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 judgements relating to the 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 procedure by which the manufacturer of a medical device can identify hazards associated with a medical device and its accessories, 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.

Medical devices — Application of risk management to medical devices

1 Scope

This International Standard specifies a procedure by which a manufacturer can identify the hazards associated with medical devices and their accessories, 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 judgements 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 system in place. However, risk management can be an integral part of a quality system (see, for example, Table G.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, or an accessory, 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]

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

2.7
medical device
any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of

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

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

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

— control of conception,

and which does not achieve its principal 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 13485:1996, definition 3.1]

2.8
objective evidence
information which can be proven true, based on facts obtained through observation, measurement, test or other means

[ISO 8402:1994, definition 2.19]

2.9
procedure
specific way to perform an activity

[ISO 8402:1994, definition 1.3]

2.10
process
set of inter-related resources and activities which transform inputs into outputs

[ISO 8402:1994, definition 1.2]

2.11
record
document which furnishes objective evidence of activities performed or results achieved

[ISO 8402:1994, definition 3.15]

2.12
residual risk
risk remaining after protective measures have been taken

[ISO/IEC Guide 51:1999, definition 3.9]

2.13
risk
combination of the probability of occurrence of harm and the severity of that harm

[ISO/IEC Guide 51:1999, definition 3.2]

2.14
risk analysis
systematic use of available information to identify hazards and to estimate the risk

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

2.15
risk assessment
overall process comprising a risk analysis and a risk evaluation

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

2.16
risk control
process through which decisions are reached and protective measures are implemented for reducing risks to, or maintaining risks within, specified levels

2.17
risk evaluation
judgement, on the basis of risk analysis, of whether a risk which is acceptable has been achieved in a given context based on the current values of society

NOTE Based on ISO/IEC Guide 51: 1999, definitions 3.11 and 3.7.

2.18
risk management
systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating and controlling risk

2.19
risk management file
set of records and other documents, not necessarily contiguous, that are produced by a risk management process

2.20
safety
freedom from unacceptable risk

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

2.21
severity
measure of the possible consequences of a hazard

2.22
verification
confirmation by examination and provision of objective evidence that specified requirements have been fulfilled

NOTE In design and development, verification concerns the process of examining the result of a given activity to determine conformity with the stated requirement for that activity.

[ISO 8402:1994, definition 2.17]

3 General requirements for risk management

3.1 National or regional regulatory requirements

Because of the wide variety of medical devices covered by this International Standard and the different national or regional regulatory requirements covering those devices, the requirements given in 3.3 and 3.4 apply as appropriate.

3.2 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 control. 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 design/development process exists, it shall incorporate the appropriate parts of the risk management process.

NOTE 1 A documented product design/development 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 A schematic representation of the risk management process is shown in Figure 1.

NOTE 3 See the bibliography.

Compliance is checked by inspection of the risk management file.

3.3 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 trained personnel (see 3.4) 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 in the risk management file.

Compliance is checked by inspection of the risk management file.

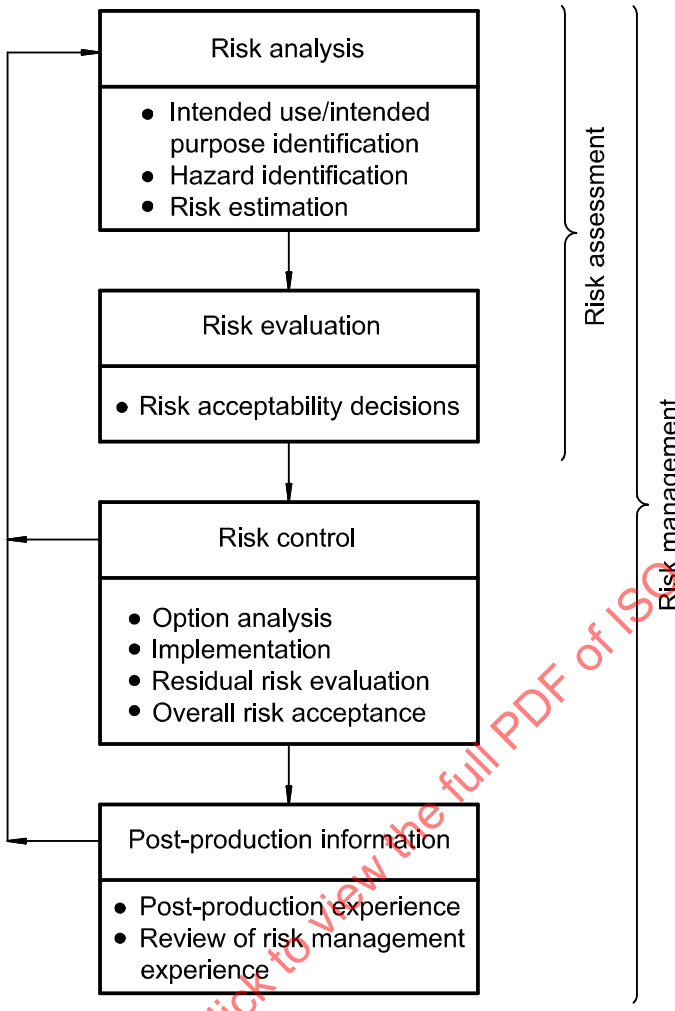

Figure 1 — Schematic representation of the risk management process

3.4 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 and its use and risk management techniques. Records of the appropriate qualifications shall be maintained.

Compliance is checked by inspection of the appropriate records.

3.5 Risk management plan

For the particular medical device or accessory 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 shall include the following:

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

b) a verification plan;

c) allocation of responsibilities;

d) requirements for review of risk management activities; and

e) criteria for risk acceptability.

NOTE The criteria for risk acceptability will do much to determine the ultimate effectiveness of the risk management process. Refer to annex E for guidance on establishing such criteria.

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.

3.6 Risk management file

For the particular medical device or accessory being considered, the results of all risk management activities shall be recorded and maintained in the risk management file.

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 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.

4 Risk analysis (Steps 1, 2 and 3 of Figure 2)

4.1 Risk analysis procedure

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 If a risk analysis is available for a similar medical device, it may be used as a reference 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.

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 or accessory 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 (Step 1)

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

NOTE 1 Annex A 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 B.

NOTE 3 Additional guidance on risk analysis techniques for toxicological hazards is given in annex C.

Compliance is checked by inspection of the risk management file.

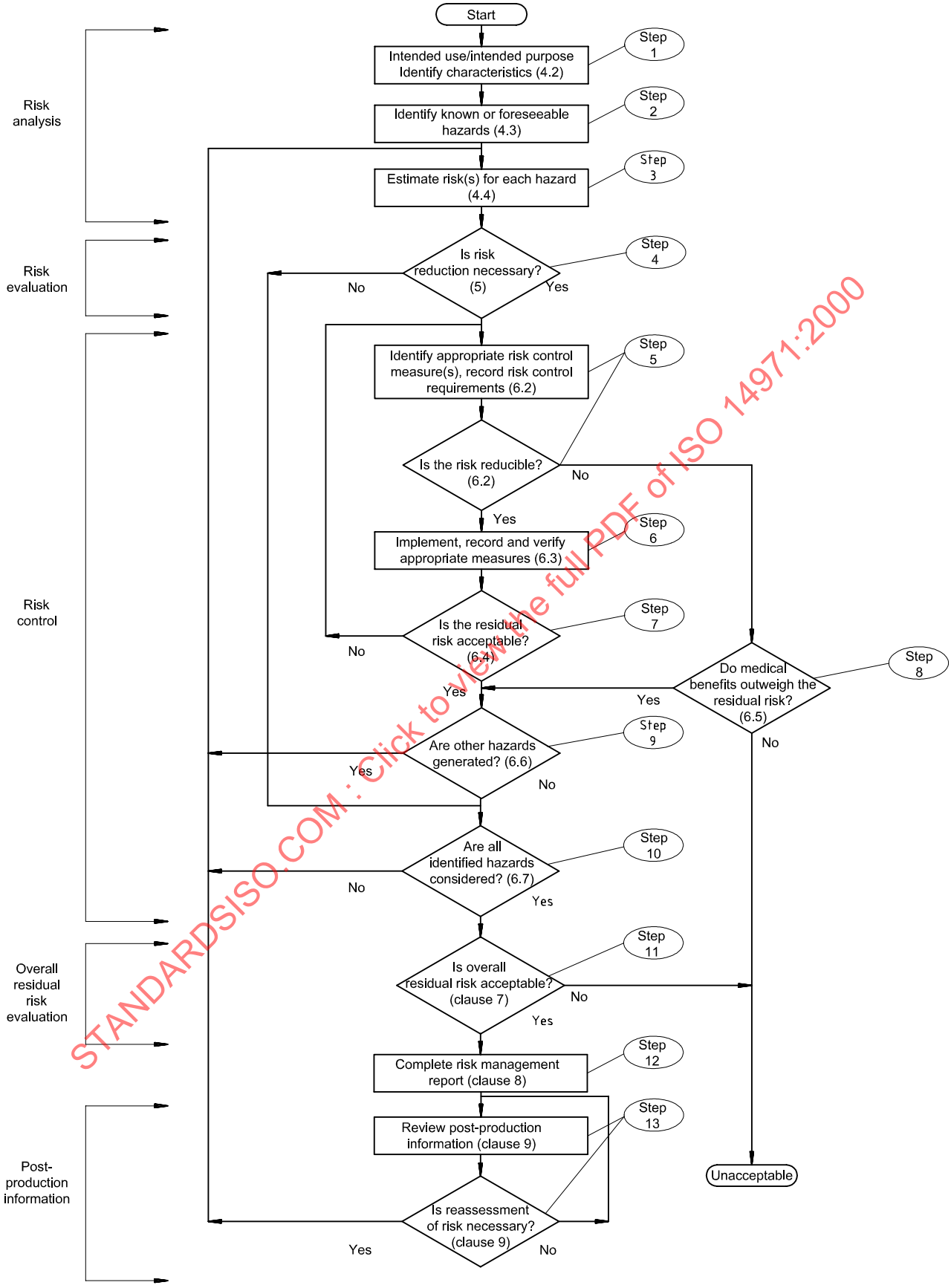

Figure 2 — Overview of risk management activities as applied to medical devices

4.3 Identification of known or foreseeable hazards (Step 2)

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 may result in a hazardous situation shall be considered and recorded.

NOTE 1 The examples of possible hazards listed in annex D, and in clause B.2 for *in vitro* diagnostic medical devices, can be used as an aide-memoire.

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 (Step 3)

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, a listing of the possible consequences of the hazard shall be prepared. The estimate of the risk(s) shall be recorded in the risk management file.

Any system used for qualitative or quantitative categorization of probability estimates or severity levels 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 may 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 annex E. Clause B.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 F.

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,

— external quality assessment schemes.

Compliance is checked by inspection of the risk management file.

5 Risk evaluation (Step 4)

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 clause E.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 (Steps 5 to 10)

6.1 Risk reduction

When risk reduction is required, the manufacturer shall follow the process 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 (Step 5)

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 descriptive safety for many medical devices. These should be consulted as part of the risk management process. See also annex G.

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 impractical, 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) (Step 6)

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

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

Compliance is checked by inspection of the risk management file.

6.4 **Residual risk evaluation** (Step 7)

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).

If the residual risk is judged acceptable, then all relevant information necessary to explain the residual risk(s) shall be placed in the appropriate accompanying documents supplied by the manufacturer.

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

6.5 **Risk/benefit analysis** (Step 8)

If the residual risk is judged unacceptable using the criteria established in the risk management plan and further risk control is impractical, 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 **Other generated hazards** (Step 9)

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 evaluation** (Step 10)

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

Compliance is checked by inspection of the risk management file.

7 **Overall residual risk evaluation** (Step 11)

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 judged unacceptable 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 does not support the conclusion that the medical benefits outweigh the overall residual risk, then the risk remains unacceptable. The results of 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** (Step 12)

The results of the risk management process shall be recorded in a risk management report. The risk management report 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 the residual risk(s) is acceptable. The risk management report shall form part of the risk management file.

NOTE This report may be held on paper or on electronic media.

Compliance is checked by inspection of the risk management report.

9 Post-production information (Step 13)

The manufacturer shall establish and maintain a systematic procedure to review information gained about the medical device or similar devices in the post-production phase. The information shall be evaluated for possible relevance to safety, especially the following:

a) if previously unrecognized hazards are present;

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

c) if the original assessment is otherwise invalidated.

If any of the above conditions is satisfied, the results of the evaluation shall be fed back as an input to the risk management process (see 4.4).

In the light of this safety relevant information, a review of the appropriate steps of risk management process for the medical device shall be considered. If there is a potential that the residual risk(s) or its acceptability has changed, the impact on previously implemented risk control measures shall be evaluated.

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

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

NOTE 2 See also 4.14 of ISO 13485:1996.

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

Compliance is checked by inspection of the risk management process documentation and the risk management file.

Annex A
(informative)

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

A.1 General

The first step in identifying hazards is to analyse the medical device for characteristics that could affect safety. 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 may emerge of where the potential hazards can be found. The following questions can aid the reader in identifying all the potential hazards of the medical device being analysed.

The list is not exhaustive, and the reader is cautioned to add questions that may have applicability to the particular medical device.

A.2 Questions

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

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?

What role is the medical device intended to play in the diagnosis, prevention, monitoring, treatment or alleviation of disease, compensation for injury or handicap, 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.27)?

A.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.

A.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.

A.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.

A.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.

A.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).

A.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.

A.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.

A.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.

A.2.10 Are measurements taken?

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

A.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.

A.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 which can be involved and the potential problems associated with such interactions, as well as patient compliance with the therapy.

A.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 discharge of chemicals, waste products and body fluids.

A.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.

A.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.

A.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.

A.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?

A.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.

A.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.

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

Factors that should be considered include ergonomic and cumulative effects.

A.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.

A.2.22 What determines the lifetime of the medical device?

Factors that should be considered include ageing and battery depletion.

A.2.23 Is the medical device intended for single use?

A.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?

A.2.25 Does installation or use of the medical device require special training?

Factors that should be considered include 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.

A.2.26 Will new manufacturing processes need to be established or introduced?

The introduction of new manufacturing processes into the manufacturer facilities has to be considered as a potential source of new hazard(s) (e.g. new technology, new scale of production).

A.2.27 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.

A.2.27.1 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.

A.2.27.2 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, and whether the controls are continuous or discrete, and the reversibility of settings or actions.

A.2.27.3 Does the medical device display information?

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

A.2.27.4 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, and sequence clarity and memorization problems, and importance of control function relative to its accessibility.

A.2.28 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.

Annex B
(informative)

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

B.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 may result from hazards associated with *in vitro* diagnostic medical device, leading or contributing to erroneous decisions. In addition, use-related hazards and their associated risks should be considered.

B.2 Identification of hazards

In addition to those aspects mentioned in annex D, 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).

B.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 C
(informative)

Guidance on risk analysis procedure for toxicological hazards

C.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 may indicate that tests should be omitted if the omission can be scientifically justified.

C.2 Estimation of toxicological risks

C.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.

C.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.

C.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.

C.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 D
(informative)

Examples of possible hazards and contributing factors associated with medical devices

D.1 General

This annex provides a non-exhaustive list of possible hazards together with contributing factors which may be associated with different medical devices. This list can be used to aid in the identification of hazards associated with a particular medical device.

D.2 Energy hazards and contributory factors

These include

— electricity,

— heat,

— mechanical force,

— ionizing radiation,

— non-ionizing radiation,

— moving parts,

— unintended motion,

— suspended masses,

— failure of patient-support device,

— pressure (e.g. vessel rupture),

— acoustic pressure,

— vibration,

— magnetic fields (e.g. MRI).

D.3 Biological hazards and contributory factors

These include

— bio-contamination,

— bio-incompatibility,

— incorrect formulation (chemical composition),

— toxicity,

— allergenicity,

— mutagenicity,

— oncogenicity,

— teratogenicity,

— carcinogenicity

— re- and/or cross-infection,

— pyrogenicity,

— inability to maintain hygienic safety,

— degradation.

D.4 Environmental hazards and contributory factors

These include

— electromagnetic fields,

— susceptibility to electromagnetic interference,

— emissions of electromagnetic interference,

— inadequate supply of power,

— inadequate supply of coolant,

— storage or operation outside prescribed environmental conditions,

— incompatibility with other devices with which it is intended to be used,

— accidental mechanical damage,

— contamination due to waste products and/or medical device disposal.

D.5 Hazards resulting from incorrect output of energy and substances

These include

— electricity,

— radiation,

— volume,

— pressure,

— supply of medical gases,

— supply of anaesthetic agents.

D.6 Hazards related to the use of the medical device and contributory factors

These include

— inadequate labelling,

— inadequate operating instructions, such as
  - inadequate specification of accessories to be used with the medical device,
  - inadequate specification of pre-use checks,
  - over-complicated operating instructions,
  - inadequate specification of service and maintenance,
— use by unskilled/untrained personnel,
— reasonably foreseeable misuse,
— insufficient warning of side effects,
— inadequate warning of hazards likely with re-use of single-use medical devices,
— incorrect measurement and other metrological aspects,
— incompatibility with consumables/accessories/other medical devices,
— sharp edges or points.

D.7 Inappropriate, inadequate or over-complicated user interface (man/machine communication)

These include

— mistakes and judgement 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.

D.8 Hazards arising from functional failure, maintenance and ageing and contributory factors

These include

— 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,

— inadequate packaging (contamination and/or deterioration of the medical device),

— re-use and/or improper re-use,

— 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.

Annex E
(informative)

Risk concepts applied to medical devices

E.1 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 is carried out (see 4.4). Quantitative risk estimation is possible when suitable data are available. Methods for quantitative risk estimation could merely include the adaptation of a qualitative method, or an alternative approach might be appropriate.

A risk chart such as Figure E.1 can be used as part of a qualitative method to define risk. Figure E.1 is an example of a risk chart and is included only to show the method. This does not imply that it has general application to medical devices. 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 may occur;

— 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 analyse risks, their components, i.e. probability and severity, should be analysed separately.

E.2 Probability

E.2.1 Probability estimation

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

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

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

— Does the hazard occur in a failure mode?

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

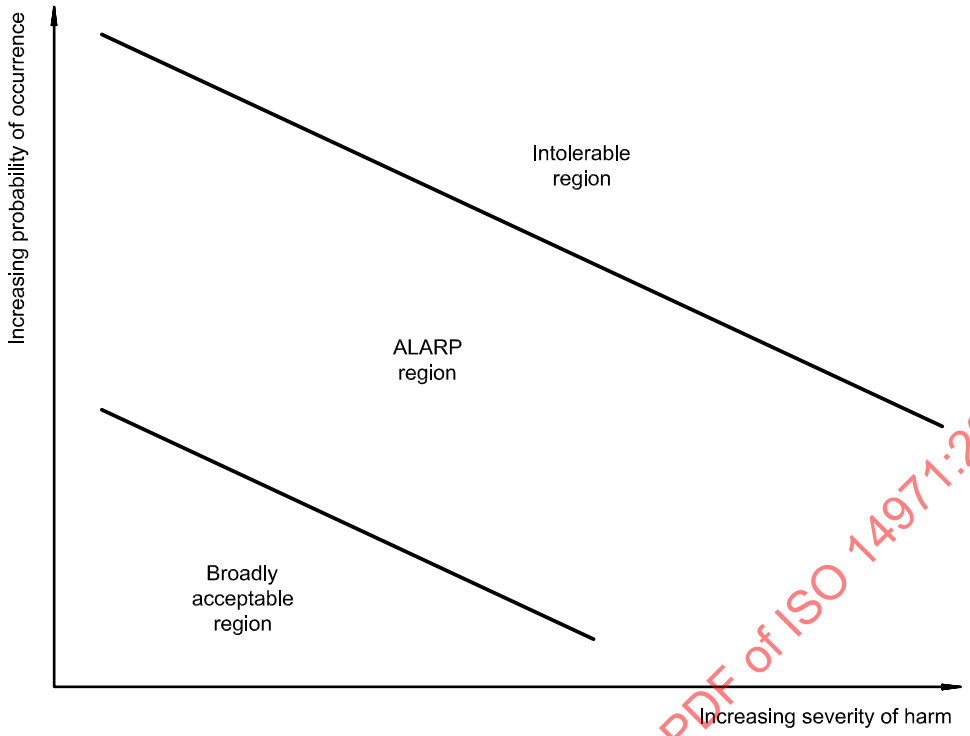

Figure E.1 — Example of a three-region risk chart

The probability of each undesired event occurring is identified at the hazard-identification stage. Three approaches are commonly employed to estimate probabilities, as follows:

— use of relevant historical data,

— prediction of probabilities using analytical or simulation techniques,

— use of expert judgement.

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 can be used as independent checks on each other, and this might serve to increase confidence in the results. When these cannot be used or are not sufficient, it might be necessary to rely on expert judgement.

Some hazards occur because of systematic rather than random failures. For example, hazards derived from software failures are due to systematic failures. For a discussion on how to address systematic failures, see E.4.3.

E.2.2 Severity levels

For a qualitative categorization of the levels of severity, the manufacturer should use descriptors appropriate for the medical device. The concept is in reality a continuum, however in practice a number of discrete levels can be used. In this case, the manufacturer decides how many categories are needed and how they are to be defined. The levels may be descriptive (e.g. negligible, marginal, critical, serious, catastrophic) or symbolic (S1, S2, etc.).

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

E.3 Risk acceptability

E.3.1 General

This International Standard does not specify acceptable risk. 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);

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

Risk should only be accepted in a particular situation if it is outweighed by benefits.

Risks can be categorized into the following three regions:

— broadly acceptable region;

— ALARP (As Low As Reasonably Practicable) region;

— intolerable region.

A three-region concept of risk is illustrated in Figure E.1. These regions will need to be customized for a particular medical device.

Examples of the use of numerical probability and severity estimates can be found in some of the standards listed in the bibliography. Users of this International Standard are urged to define probability and severity categories applicable to their own particular application.

E.3.2 Broadly acceptable region

In some cases, a risk is so low that it is negligible in comparison with other risks and in view of the benefit of using the medical device. In such cases, the risk is acceptable and risk control need not be actively pursued.

E.3.3 ALARP region

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

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

a) technical practicability, and

b) economic practicability.

Technical practicability refers to the ability to reduce the risk regardless of cost. 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 may suffice.

E.3.4 Intolerable region

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

E.3.5 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), and then the risk and benefit should be compared. If the risk is outweighed by the benefit, then the risk may be accepted. If the risk is not outweighed by the benefit, then it is unacceptable, and the design should be abandoned.

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

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?

E.4 Cause of failure

E.4.1 Failure types

A hazardous situation can result from the failure of a system. There are two possible types of failure:

— random failures, and

— systematic failures.

E.4.2 Random failure

For many events, a statistical probability of failure can be assigned (e.g. the probability of failure of an assembly is often estimated from the failure probabilities of the components which make up the assembly). In this case, a numerical value can be given for the probability of failure. An essential presumption is that the failures are random in nature. Hardware is assumed to fail either in a random or in a systematic manner. Software is assumed to fail in a systematic manner.