



GUIDE 63

**Guide to the development and
inclusion of safety aspects in
International Standards for
medical devices**

Second edition 2012

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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 2.

Draft Guides adopted by the responsible Committee or Group are circulated to the member bodies for voting. Publication as a Guide 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.

ISO/IEC Guide 63 was prepared jointly by ISO/TC 210, *Quality management and corresponding general aspects for medical devices*, and IEC/SC 62A, *Common aspects of electrical equipment used in medical practice*, in a Joint Working Group, *Application of risk management to medical devices*.

This second edition cancels and replaces the first edition (ISO/IEC Guide 63:1999), which has been technically revised.

Introduction

ISO/IEC Guide 51 was the first of a series of guides intended to provide a harmonized approach to the concept of safety when preparing International Standards. ISO/IEC Guide 51 anticipated the need for sectoral guides such as this Guide. Consistent with ISO/IEC Guide 51, additional guidance might be needed for sectors within the broad category of medical devices.

The concept of safety, including safety-related performance and usability, is closely related to safeguarding the integrity of the patients who are the subjects of medical care, as well as that of those persons who are giving the care and any other persons. As medical devices and medical systems have become more complex, the diligence required to ensure their safety has similarly increased.

As different circumstances warrant different approaches to ensuring safety, it is impossible to provide precise requirements and recommendations that apply to every case. However, these guidelines, when followed on a judicious “use when applicable” basis, will help in developing reasonably consistent standards.

Guide to the development and inclusion of safety aspects in International Standards for medical devices

1 Scope

This Guide provides guidance to standards writers on how to include safety aspects in the development of medical device safety standards intended to be used within the risk management framework established in ISO 14971. It expands on the concepts developed in ISO/IEC Guide 51 to include safety-related performance and usability.

This Guide is intended to be read in conjunction with ISO/IEC Guide 51 and ISO 14971.

2 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

2.1

accompanying document

document accompanying a medical device and containing information for those accountable for the installation, use and maintenance of the medical device, the operator or the user, particularly regarding safety

[ISO 14971:2007, definition 2.1]

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 3.3]

2.3

hazard

potential source of harm

NOTE The term hazard can be qualified in order to define its origin or the nature of the expected harm (e.g. electric shock hazard, crushing hazard, cutting hazard, toxic hazard, fire hazard, drowning hazard).

[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 hazards

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

2.5

intended use

intended purpose

use for which a product, process, or service is intended according to the specifications, instructions and information provided by the manufacturer

[ISO 14971:2007, definition 2.5]

2.6

life cycle

all phases in the life of a medical device, from the initial conception to final decommissioning and disposal

[ISO 14971:2007, definition 2.7]

2.7

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 or put into service, regardless of whether these operations are carried out by that person or on that person's behalf by a third party

NOTE 1 Attention is drawn to the fact that the provisions of national or regional regulations can apply to the definition of manufacturer.

NOTE 2 For a definition of labelling, see ISO 13485:2003, definition 3.6.

[ISO 14971:2007, definition 2.8]

2.8

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

NOTE 1 This definition has been developed by the Global Harmonization Task Force (GHTF).

NOTE 2 Products, which could be considered to be medical devices in some jurisdictions, but for which there is not yet a harmonized approach, are

- aids for disabled/handicapped people,
- devices for the treatment/diagnosis of diseases and injuries in animals,
- accessories for medical devices,
- disinfection substances,
- devices incorporating animal and human tissues which can meet the requirements of the above definition but are subject to different controls.

NOTE 3 Adapted from ISO 13485:2003, definition 3.7, and ISO 14971:2007, definition 2.9.

2.9

residual risk

risk remaining after risk control measures have been taken

NOTE 1 ISO/IEC Guide 51:1999, definition 3.9, uses the term “protective measures” rather than “risk control measures”.

NOTE 2 Adapted from ISO 14971:2007, definition 2.15.

2.10

risk

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

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

2.11

risk analysis

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

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

NOTE Risk analysis includes the examination of different sequences of events that can produce hazardous situations and harm.

2.12

risk control

process in which decisions are made and measures implemented by which risks are reduced to, or maintained within, specified levels

[ISO 14971:2007, definition 2.19]

2.13

risk estimation

process used to assign values to the probability of occurrence of harm and the severity of that harm

[ISO 14971:2007, definition 2.20]

2.14

risk evaluation

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

[ISO 14971:2007, definition 2.21]

2.15

risk management

systematic application of management policies, procedures and practices to the tasks of analysing, evaluating, controlling and monitoring risk

[ISO 14971:2007, definition 2.22]

2.16

safety

freedom from unacceptable risk

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

2.17

severity

measure of the possible consequences of a hazard

[ISO 14971:2007, definition 2.25]

2.18

usability

characteristic of the user interface that establishes effectiveness, efficiency, ease of user learning and user satisfaction

[IEC 62366:2007, definition 3.17]

2.19

use error

act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user

NOTE 1 Use error includes slips, lapses, and mistakes.

NOTE 2 See also IEC 62366:2007, Annex B and D.1.3.

NOTE 3 An unexpected physiological response of the patient is not in itself considered use error.

[IEC 62366:2007, definition 3.21]

2.20

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 tests and demonstrations, and
- reviewing documents prior to issue.

[ISO 9000:2005, definition 3.8.4]

3 Principles for preparing medical device safety standards

3.1 General considerations

The goal of medical device safety standards is to support the development and production of medical devices with a predictable, consistent level of safety.

To achieve this goal, medical device safety standards should

- a) assist manufacturers in the design and production of safe and effective medical devices,
- b) assist manufacturers, certification bodies, testing laboratories or test houses, and regulatory authorities in assessing compliance with legal and market requirements, and
- c) assist health care providers in managing risks associated with the use of medical devices.

To produce medical device safety standards that are well suited to assisting the stakeholders listed above, the standards writers are encouraged to employ a risk-based framework (see Clause 4).

3.2 Scope of safety standards

The planning and development of medical device safety standards require a global approach that includes manufacturers, users, regulatory authorities and other stakeholders. Close coordination within and among committees responsible for different medical devices is necessary to create a coherent approach to the treatment of safety in the preparation of standards. Defining the scope of safety standards will ensure that each standard is restricted to specific aspects and makes reference to standards of wider application for all other relevant aspects. Such a hierarchy is built on:

- **basic safety standards**, including fundamental concepts, principles and requirements with regard to general safety aspects applicable to all kinds or a wide range of products, processes and services (basic safety standards are sometimes referred to as horizontal standards);
- **group safety standards**, including safety aspects applicable to several, or a family of, similar products, processes or services dealt with by two or more technical committees or subcommittees, making reference, as far as possible, to basic safety standards;
- **product safety standards**, including all necessary safety aspects of a specific, or a family of, product(s), process(es), or service(s) within the scope of a single technical committee or subcommittee, making reference, as far as possible, to basic safety standards and group safety standards (product safety standards are sometimes referred to as vertical standards).

This hierarchy is set out in ISO/IEC Guide 51:1999, 7.1.

Safety requirements for medical devices may be incorporated in different types of standards (see 3.3) that may be found at any appropriate level in the hierarchy described above.

3.3 Types of standards

3.3.1 Product standards

These can be

- standards that state safety or performance parameters and include reference test methods that can be used to demonstrate conformance to those parameters, or
- disclosure and test method standards where adherence to declared pass/fail criteria are necessary for safety and performance.

See Clause A.1 for a discussion of how product standards can contribute to the safety and the effectiveness of medical devices.

3.3.2 Process standards

These can be

- a) quality system standards that establish a framework within which the manufacturer is able to design, develop and produce medical devices that consistently meet specifications, or
- b) standards that establish a framework within which the manufacturer is able to design and develop medical devices of consistent safety and effectiveness, or
- c) standards for processes used for the design, development or production of safe and effective medical devices (e.g. sterilization, biological evaluation, clinical investigation).

See Clause A.2 for a discussion of how process standards can contribute to the safety and the effectiveness of medical devices.

Some types of standards cannot be easily allocated to one of these categories since they combine properties of product standards and process standards. Examples are described in 3.3.3 and 3.3.4.

3.3.3 Installation and environmental standards

These standards are generally appropriate for large systems and active medical devices. These can be

- a) construction and installation standards (e.g. X-ray shielding, electrical wiring),
- b) system standards that address the proper precautions and procedures for interconnection of multiple devices into a single system,
- c) commissioning standards that address the proper testing and inspection procedures to apply to permanently installed equipment and systems prior to initial use, or
- d) environmental standards that address precautions and testing to ensure that a medical device does not negatively affect its environment and that the environment does not degrade or otherwise impair the performance of a medical device (e.g. electromagnetic compatibility standards).

3.3.4 In-process standards

These can be

- a) routine in-service testing standards to ensure that the safety of active medical devices is maintained over the useful life of the equipment, or
- b) quality assurance and calibration standards to ensure the continued proper function and accuracy of medical devices where relevant to safety.

3.4 Taking a practical view of safety

Risk must be balanced against other demands on the product, process or service. These other demands include benefit, suitability and cost. Standards writers should remember that the level of required effort from the manufacturer (e.g. for required documentation or testing) should be scaled to the level of risk.

Because zero risk is unattainable, safety is defined as freedom from unacceptable risk. Although zero risk is an ideal to pursue, its attainment should not be expected. The realistic expectation is to choose risk acceptability criteria that take into account available information, such as the generally accepted state of the art and known stakeholder concerns, and that result in a high level of safety and protection of health.

In evaluating the safety of medical devices, it is also necessary to consider that certain medical devices, because of their means of operation, composition or the circumstances of their use, carry with them an inherent risk that cannot be eliminated without degrading their effectiveness.

Differences exist in medical and health practices among cultures including judgments about the safety of medical devices. Furthermore, what is considered safe within a culture evolves over time as technologies and social values change. These issues can often be addressed by identifying the specific conditions under which a technical requirement applies.

Standards writers should focus on requirements relevant to medical device safety or to the safe use of the medical device, and avoid features or functions that are not essential to safety.

3.5 Managing risks

The risk management process for medical devices includes the following:

- a) establishing risk acceptability criteria;
- b) identifying hazards and the scenarios that result in hazardous situations;
- c) estimating the associated risks;

- d) identifying risk control measures to reduce each risk, as needed, to meet the risk acceptability criteria;
- e) implementing risk control measures;
- f) verifying the effectiveness of the risk control measures.

This risk management process is described more comprehensively in ISO 14971.

Standards development should be based on hazard identification. The goal of standards development is to produce standards that specify methods for hazard identification or measures to control risks such that risk acceptability criteria are met (see 3.6).

These considerations should then be taken into account as the standards writers determine the appropriate requirements to be included in the standard.

Clause 5 provides an overview of how medical device safety standards can facilitate the implementation of a risk management system that is compliant with ISO 14971.

3.6 Risk acceptability criteria

The goal of medical device safety standards is to support the development of medical devices with an acceptable level of risk. Medical device safety standards should provide practical criteria, such as design limits and performance criteria, when describing the acceptability criteria.

3.7 Risk control methods/methodology

Medical device safety standards should determine methods/methodologies appropriate to the control of risks associated with the related medical devices. This may include aspects of performance, design, manufacturing process, installation, servicing, etc. based upon a risk management approach throughout the entire life cycle.

3.8 Coordination of medical device safety standards

The development of each new medical device safety standard needs to be viewed in the context of existing medical devices and standards, as well as national, regional and international laws. New standards should make use of the body of existing standards, whenever relevant, either by reference or by reproduction of text where this is justified by convenience or clarity (see ISO/IEC Directives, Part 2, 2011, Clause A.7).

3.9 Regulatory implications

Safety and effectiveness of medical devices, whose sale and use is regulated in many countries, are of particular concern to regulatory authorities.

Standards are often cited in regulations and legislation, in which case the standards themselves become legally binding. Alternatively, there are systems where a medical device that complies with a specified standard is “deemed to comply” with the regulations.

Standards may also be cited in litigation as what may reasonably be expected by society, and thus used to establish compliance with these expectations.

Standards writers should be aware of the possible legal and regulatory implications of the standard they develop.

4 Risk-based framework for developing a medical device safety standard

4.1 General

In applying ISO 14971 to medical device risks, the risk control measures selected can include both product design features and process controls. The choice of a risk control measure is dependent upon the effectiveness and feasibility of the available risk control measures. Similarly, in applying ISO 14971 principles to the development of standards, the type of standard may be either a product or a process standard or a combination of the two types (see 3.3). The choice is dependent on the medical device or process that is analysed and the resulting risks that are identified. The scope of the standard should reflect this choice.

Clause 4 follows the procedural steps of ISO 14971. These enable the standards writers to take a systematic approach when identifying the need for a safety standard and the risk controls that should be included in the standard to manage risks. These steps can also aid in the preparation of a New Work Item Proposal for a new project. Product and process standards may be used as different approaches to control product risks. Although Clause 4 is product-oriented, it applies equally to an effort that might lead to a process standard. There are two reasons for this:

- although the management of different types of risk may involve processes that need to be controlled using different procedures, models or methods, it is necessary for process standards writers to ensure that product risk management objectives can be met;
- the value of a process standard is determined by its usefulness in meeting product risk management objectives.

Thus, 4.2 to 4.8 may be viewed as aiding in the problem identification phase, 4.9 as aiding in the decision on the need for managing risks with a standard and 4.10 as aiding in decisions on the methods of risk control, e.g. safety features, control of processes or process parameters, safety information, etc.

4.2 Management of the risk-based framework

When deciding on the need for a medical device safety standard, the initial task, independent of the type of standard, is to

- determine the application of the medical device or the process,
- identify the characteristics related to the safety of the medical device or related process,
- identify the hazards and hazardous situations associated with the life cycle of the medical devices and their use,
- determine whether the risks posed by those hazards need to be controlled, and
- determine those risks that can be controlled by a standard.

4.3 Application and characteristics

Determination of the application of the medical devices or processes under consideration includes the following:

- a) intended medical indication [e.g. condition(s) or disease(s) to be screened, monitored, treated, diagnosed, or prevented];
- b) intended patient population (e.g. age, weight, health, condition);
- c) intended part of the body or type of tissue applied to or interacted with;

- d) intended user profile;
- e) intended environment, conditions and methods of use;
- f) preparatory and service procedures prior to use (e.g. sterilization, assembly, calibration).

Characteristics of the medical device or process can influence the safety of patients and users and should be taken into account when considering the need for a standard. Typical characteristics include the following:

- sterility;
- biocompatibility;
- pyrogenicity;
- reliability;
- usability;
- functionality;
- sensitivity and specificity;
- electrical safety;
- mechanical strength;
- radiation safety.

In order to systematically identify hazards and hazardous situations, it is important to define the medical devices or processes under consideration in sufficient detail to establish where safety issues can arise.

4.4 Identification of hazards and hazardous situations

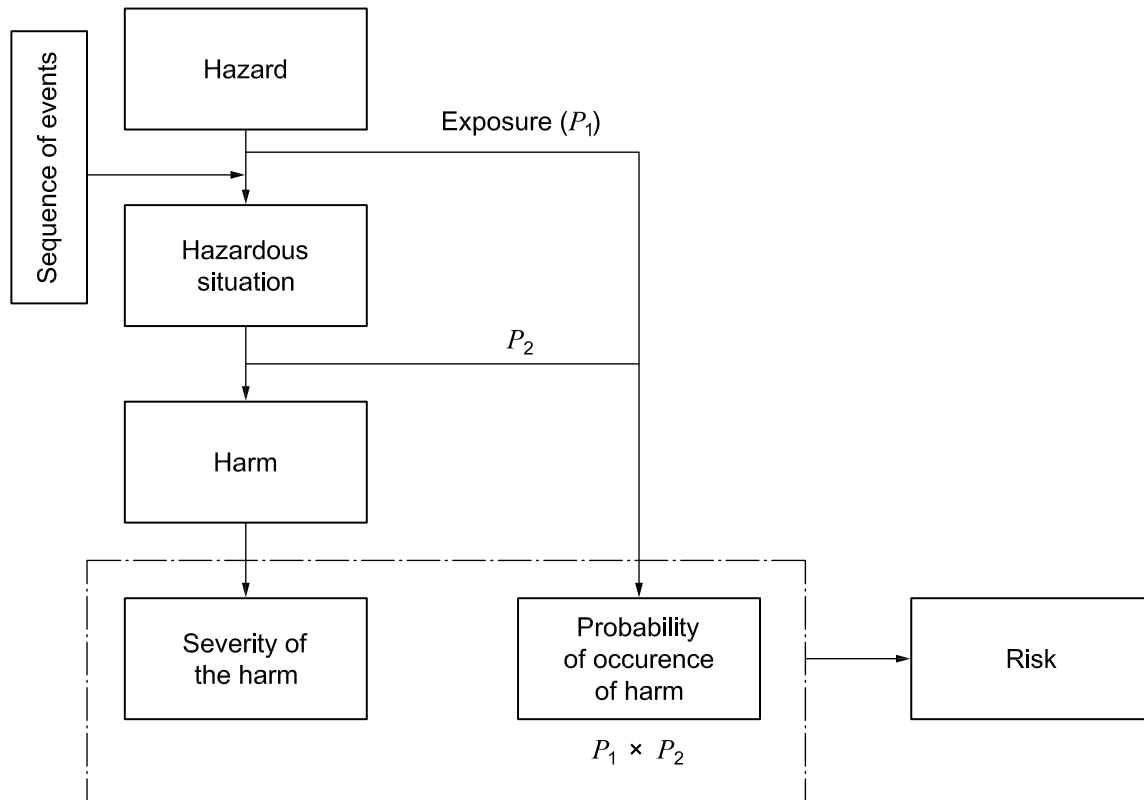
Hazard identification usually involves the following steps:

- identification of possible hazards related to the way in which a medical device is normally used or foreseeably misused; and
- identification of sequences of events which could result in a hazardous situation.

After the identification of known and foreseeable hazards associated with the medical device in both normal and fault conditions, the foreseeable sequences of events that can produce hazardous situations and harm need to be considered. Figure 1¹⁾ depicts these relationships.

A hazard cannot result in harm until such time as a sequence of events or other circumstances (including normal use) lead to a hazardous situation or exposure to harm. At this stage, the risk can be assessed by estimating both the severity and probability of occurrence of harm that could result. Note that foreseeable events related to fault conditions may include activities related to the manufacturing, installation or servicing of a medical device.

1) Originally published in ISO 14971:2007 as Figure E.1.



Key

- P_1 probability of a hazardous situation occurring
- P_2 probability of a hazardous situation leading to harm

Figure 1 — Pictorial representation of the relationship of hazard, sequence of events, hazardous situation and harm

4.5 Types of hazards and hazardous situations

4.5.1 General

For a general discussion of hazards and hazardous situations, refer to ISO 14971:2007, Annex E.

4.5.2 Medical device-related hazards and hazardous situations

To a great extent, the possible medical device-related hazards depend on the nature of the medical device. Since it is not possible to ensure that a medical device will not fail, the standard should recognize the hazards of the medical devices as they pertain to the condition, health and safety of the patient and the health and safety of the user. The preferred result in the event of a failure is failure to a safe mode (fail-safe). Alternatively, when possible or practicable, the medical device should give warning prior to failure or at the time of failure. Warnings and alarms are more easily included on active medical devices, but are not impossible to include in many inactive medical devices.

Some examples of device-related hazards and hazardous situations are the following:

- a) failure of a medical device to perform its intended function, e.g. failure of a defibrillator to deliver the proper energy, mechanical failure of a cardiac valve;

- b) incorrect performance of a medical device, e.g. an automatic external defibrillator delivering output at an inappropriate time;
- c) for active medical devices, hazards due to the energies involved in the proper functioning of the medical device, e.g. flow of current through an unintended path through the patient or user, excessive or inadequate heating or cooling of a patient or part of a patient;
- d) micro-organisms transmitted by a non-sterile medical device, e.g. caused by improper sterilization or failure of a sterile barrier;
- e) hazards incidental to the function of the medical devices, e.g. fire caused by the ignition of flammable materials in the vicinity of the medical device;
- f) hazardous situations arising from the incorrect reading of a medical device's output, e.g. interpretation of the results of an *in vitro* diagnostic test or the diagnostic output, reading or alarm from vital signs monitoring the equipment;
- g) hazardous situations arising from mechanical failure of a medical device or its ancillary equipment, e.g. collapse of a component of an X-ray table, failure of side-rails on a hospital bed;
- h) hazards related to the toxicity of materials used in the medical device or leached from the medical device, or lack of biocompatibility of the component materials of the medical device; these hazards may be immediate (occurring soon after initial use of the medical device) or long-term (arising only after prolonged exposure to the medical device);
- i) hazardous situations arising from the interconnection of incompatible devices.

4.5.3 Patient-related hazards and hazardous situations

Some hazards and hazardous situations are specifically related to the patient and the patient environment. Some examples are the following:

- a) inability of the patient or user to detect the presence of certain hazards, such as ionizing or high-frequency radiation;
- b) absence of normal reaction by the patient resulting from his or her physical condition, such as a patient who is ill, unconscious, sedated or anaesthetized;
- c) patient's decreased state of immunological resistance that may not be able to overcome infectious attack;
- d) environmental conditions in patient areas that may present a combination of humidity and fire or explosion hazards related to the presence of pure oxygen, nitrous oxide and other anaesthetic media and cleaning agents;
- e) patient allergy or other hypersensitivity to a material used in a medical device, e.g. natural rubber latex.

4.5.4 Use-related hazards and hazardous situations

Some hazards and hazardous situations are specifically related to the application of the medical device by the user. Some examples are the following:

- a) incorrect preparatory and service procedures prior to the use of a medical device;
- b) use of a medical device for the treatment of a condition for which it is not intended by the manufacturer;
- c) use of a medical device when the user is confused, distracted or fatigued;
- d) use of a medical device by a non-expert user or by an untrained person, e.g. home-use diagnostics.

4.5.5 Occupational exposure to hazards and hazardous situations

In the use, service or repair of certain medical devices, the user or other persons may be exposed to infectious substances, hazardous chemicals or radiation, or other occupational hazards. The risk to the user or other persons presented by these exposures must be acceptable.

4.6 Systematic or random nature of risks

4.6.1 General

The presence of hazards and the occurrence of hazardous situations could be systematic or random; therefore, risks could be systematic or random.

Standards writers should address both systematic and random risks.

Standards writers should also be aware that some hazards and the occurrence of hazardous situations can be related to either a systematic or a random event. For example, a toxic substance could be on a medical device resulting from a systematic flaw in the production process (e.g. insufficient washing steps, insufficient aeration after sterilization). On the other hand, random variations in a raw material or introduced during processing might also lead to the presence of toxic substances.

4.6.2 Risks arising from systematic events

Confidence in risk estimates is enhanced when a quantitative estimate of the probability of occurrence of harm can be made on the basis of accurate and reliable data or when a reasonable qualitative estimate is possible. However, this is not always achievable. For example, the probabilities of systematic faults are extremely difficult to estimate. When the accuracy of the probability estimate is in doubt, it is often necessary to establish a broad range for the probability, or determine that it is no worse than some particular value. Examples where probabilities are very difficult to estimate include the following:

- a) software failure;
- b) human behaviour, such as use error caused by inadequate design or by errors in the instructions for use;
- c) complex situations;
- d) novel medical applications, backed by limited clinical study data.

In the absence of enough data on the probability of occurrence of harm, it is not possible to reach any risk estimate, and it is usually necessary to evaluate the risk on the basis of the nature of the harm alone. Appropriate risk control may take into account the level of severity. It is often appropriate to determine the required rigour of risk control by considering the severity of the consequence of systematic event modes and the effect of risk control measures external to the medical device. The greater the consequence and the less effective the external risk control measures, the higher the required rigour of the relevant risk control.

Examples of risk control measures may include the following:

- rigour of applied processes in design development and manufacturing: it is usually assumed that the more rigorous the processes used in the design and development or manufacturing, the lower the probability of systematic faults being introduced or remaining undetected;
- applying redundancy of risk control measures: although probability estimations may be impossible for any single risk control measure, more than one independent risk control measure usually increases confidence in the overall protection;
- reducing the time window within which two or more independent events contributing to a hazardous situation and subsequent harm need to happen: detailed measures could range from periodic self-checks to periodic maintenance;

- applying processes and mechanisms for the continuous monitoring of critical parameters, and subsequent evaluation and corrective action.

4.6.3 Risks arising from random events

For many events, a numerical value can be given for the probability that the fault will occur. A quantitative estimate can only be applied if sufficient information is known about the hazard and the circumstances affecting the probability of the hazardous situation occurring.

Some examples of random faults are the following:

- failure of a part such as an integrated circuit in an electronic assembly;
- contamination of an IVD reagent leading to its deterioration, thus causing incorrect results;
- presence of an infectious agent in or on a medical device;
- presence of a toxic substance in or on a medical device: the risk arising from the leaching of a toxic substance from a medical device can be estimated and evaluated using ISO 10993-17, which can provide assurance that the degree of exposure anticipated from the use of the medical device is lower than that likely to cause harm to health;
- use error resulting from slips, lapses and mistakes.

4.7 Risk estimation

4.7.1 General

This Guide does not suggest that standards writers use a particular tool or method for estimating risk. In principle, there is no preference for quantitative versus qualitative estimation of the probability of occurrence of harm.

Risk estimation performed by standards writers should consider available data representing the state of the art to obtain a reliable set of requirements. Preference should be given to published validated data specific for the application of the medical device under consideration. Reference to these data should be included in the standard.

The results of risk estimation activities should be explained in such detail that traceability back to the data sources used is established.

Where standards writers believe there is a safety issue that needs to be addressed in the standard they should document their assumptions in the rationale.

4.7.2 Components of risk

The concept of risk has two components, which should be analysed separately:

- a) the probability of occurrence of harm;
- b) the severity of that harm.

Risk estimation should examine, for example, the following:

- the nature and severity of the harm that could result;
- the sequence of events that could lead to a hazardous situation occurring;

- the probability of a hazardous situation arising and leading to harm (see Figure 1); and
- the initiating event or circumstance.

4.7.3 Quantitative versus qualitative

Generally speaking, medical device regulations express severity of harm qualitatively, e.g. when criteria for incident reporting or product recall are defined. As medical device safety standards may be the reference for manufacturers and regulatory authorities, the use of comparable qualitative levels may enhance the value of medical device safety standards for design and vigilance related use.

Quantitative probability estimates of occurrence of harm may be limited to those factors contributing to the overall probability estimates, which are of random nature and which can be backed by valid statistical data. One should be aware that the probability of systematic events (see 4.6.2) cannot be demonstrated easily by numerical results.

4.8 Risk acceptability criteria

4.8.1 General

It is important for standards writers to establish risk acceptability criteria suitable for use in evaluating the appropriateness of the requirements in the standard.

4.8.2 Establishing criteria

Methods of determining acceptable risk include, but are not limited to, the following:

- use of applicable standards representing the generally accepted state of the art, and including requirements sufficient for the demonstration of acceptable risk;
- comparing levels of risk evident from medical devices already in use, being considered state of the art;
- use of expert opinion;
- use of scientific research results, including clinical data.

4.8.3 Generally accepted state of the art

“Generally accepted state of the art” is used here to mean what is currently and generally accepted as good practice. “Generally accepted state of the art” does not necessarily imply the most technologically advanced solution.

4.8.4 Stakeholder concerns

It is well established that the perception of risk often differs from empirically determined risk estimates. Thus, the perception of risk from a wide cross-section of stakeholders should be taken into account when deciding what risk is acceptable. To meet the expectations of public opinion, it might be necessary to give additional weighting to some risks. In some cases, the only option could be to consider that identified stakeholder concerns reflect the values of society and that these concerns have been taken into account when the manufacturer has used the methods listed above.

4.8.5 Societal expectations

The perception of risk may differ from society to society, and this should be taken into account. Nevertheless, it would be assumed by the approval process of a medical device safety standard that differing societal expectations are included once the standard is accepted.

4.9 Risk evaluation

Using the risk acceptability criteria established in 4.8, the standards writers decide if the risks under consideration need to be controlled. If a risk needs to be controlled, the standards writers determine if a product or process standard is an appropriate risk control.

4.10 Risks to be controlled by the standard

4.10.1 General

Risk control measures can reduce the severity of the harm or reduce the probability of occurrence of the harm, or both. When determining which control measures can be included in the standard to deal with the risks identified in 4.4, it is recommended that the general methods available for reducing risk be considered first. Such methods include the following:

- a) proper design, taking into account potential risk and means for avoiding or reducing them;
- b) manufacture of medical devices in accordance with an appropriate system or process, such as controlled manufacturing process or quality systems which address risk;
- c) the choice of the appropriate medical device by the user, which in turn depends on the manufacturer providing a clear description of the intended use of the medical device;
- d) the user's understanding of the medical device, which may depend on training or appropriate and complete equipment markings, instructions for use and warnings provided by the manufacturer (this is particularly important in the case of home-use medical devices);
- e) identification and use of compatible accessories;
- f) when necessary, maintenance of the sterility of the medical device and of an appropriate sterile field in which to use the medical device;
- g) appropriate preventive maintenance and competent repair service.

These considerations should lead to requirements specific to the product or process to which the standard applies, so that the standard can take an appropriate role in helping to mitigate the risks related to this product or process.

4.10.2 Hierarchical approach to risk control

When deciding on the risk control measure(s) that are appropriate for reducing the risk(s) to an acceptable level, the following risk control options should be applied in the priority order listed:

- a) inherent safety by design;
- b) protective measures, including
 - alarms in the medical device itself, or
 - in the manufacturing process;
- c) information for safety.

4.10.3 Residual risks

4.10.3.1 General

After establishing a set of risk control measures, it should be determined whether the implemented measures can be expected to make the risk acceptable. If this is not the case, additional risk control measures should be considered. This iterative procedure should be continued until the risk is reduced to within the acceptable levels.

The user of the standard should be provided with relevant information on residual risks so that the user can make informed decisions as to whether he or she considers the standard sufficient for his or her particular product or process.

All requirements of a standard should be based on an objective risk assessment which demonstrates that the residual risks are acceptable.

4.10.3.2 Verification of effectiveness

Control measures and their associated test methods, which are prescribed in standards, should be verified for their effectiveness prior to issuing the standard. Part of this verification can come from scientific literature, or else the standards writers can decide to set up an interlaboratory study.

4.10.3.3 Validation that user needs are met

Validation that user needs are met is obtained through the international consensus process when the standard is sent to all stakeholders for several rounds of voting and comments.

4.10.3.4 Impact of introduced risk control measures

Standards writers should consider the impact of introduced risk control measures on the medical device and whether new risks are introduced by these measures that could change the initial risk assessment. For example, the standards writer should assess the impact of a risk control measure on the usability of the medical device.

4.11 Conclusion

Following the above steps will facilitate the development of a systematic, risk-based product or process standard. In addition, this approach facilitates the implementation of a risk management system compatible with ISO 14971.

5 Facilitating the implementation of ISO 14971 through product or process standards

5.1 Product standards

If a product standard specifies requirements that are intended to control the risk(s) associated with a medical device, the following should be provided:

- a rationale that supports the setting of limits, constructional details, hazardous circumstances, and why a solution is considered safe (e.g. by reference to scientific literature);
- a scope that clearly specifies the products, and their intended uses, to which the standard applies;

- test methods and limits that ensure that risks are reduced to acceptable levels, which include at least the following considerations:
 - intended medical indication [e.g. condition(s) or disease(s) to be screened, monitored, treated, diagnosed, or prevented];
 - intended patient population (e.g. age, weight, health, condition);
 - intended part of the body or type of tissue applied to or interacted with;
 - intended user profile;
 - intended conditions and methods of use;
 - preparatory and service procedures prior to use (e.g. sterilization, assembly, calibration);
 - service and maintenance procedures during the lifetime of the medical device.

The information above will allow manufacturers to determine how well the requirements of the standard satisfy their needs for risk control.

5.2 Process standards

If a process standard specifies requirements that are intended to control the risk(s) associated with a medical device, the standard should provide

- a rationale explaining how the application of the standard will reduce risk to an acceptable level as required by ISO 14971,
- methods for risk reduction and methods for generating verifiable results needed to determine that residual risk is acceptable, and
- methods for establishing goals (e.g. usability goals described in IEC 62366) that, when reached, are considered to lead to acceptable residual risk.

The process standard should provide this information in order to fulfil the requirements of ISO 14971 for risk estimation, risk control and risk control measure verification. Some process standards also include process validation steps for manufacturing processes, but process validation as such is not required by ISO 14971. Process validation may or may not demonstrate that risk reduction was sufficient to meet acceptability criteria.

The information above will allow manufacturers to determine how well the requirements of the standard satisfy their needs for risk control.

5.3 Overview of the application of medical device safety standards in an ISO 14971 framework

Reference should be made to Table 1 for general guidance on how process and product safety standards can facilitate implementation of the risk management requirements in ISO 14971. If the process or product safety standard does not specify measurable parameters and acceptable limits, it needs to specify the method for the manufacturer to develop those acceptable limits or it should invoke the use of ISO 14971 to establish appropriate acceptability criteria. Standards writers should take care only to invoke the use of the ISO 14971 process when this will create more efficiency as well as safety.

Table 1 — Guidance on how process and product safety standards can facilitate implementation of the risk management process

ISO 14971 clause/subclause	Product safety standard	Process standards
3.2 Management responsibilities	May be applicable in part.	May define additional responsibilities and tasks for management.
3.4 Risk management plan	May help to establish risk acceptability criteria.	May provide procedures for the planning of risk management.
3.5 Risk management file	Define specific content to be placed in the risk management file.	
4.2 Identification of intended use	May identify the intended use and reasonably foreseeable misuse of products and processes covered by the standard and the characteristics related to safety addressed by the standard.	
4.3 Identification of hazards	May identify known and foreseeable hazards associated with the medical device to be considered in a medical device risk analysis.	May provide formal procedures to identify known and foreseeable hazards associated with the medical device.
4.4 Estimation of the risk(s) of hazardous situations	May provide information about the degree of severity of harm or the probability of occurrence of harm, if hazardous situations occur, which may be used by the manufacturer in medical device risk analysis.	May provide specific information or procedures to systematically gather information about the degree of severity of harm or the probability of occurrence of harm, if hazardous situations occur.
5 Risk evaluation	The limits defined in the standard typically mirror the generally accepted state of the art.	May provide methods or procedures on how to evaluate and determine the acceptability of risk.
6.2 Risk control option analysis	May provide specific risk control options that can be implemented in the manufacturer's medical device design that are considered to be effective in reducing the risk.	May provide specific risk control options that can be implemented by the manufacturer and that are considered to be effective in reducing the risk.
6.3 Implementation of risk control measure(s)	May provide specific tests that verify the effectiveness of the risk control measure(s).	May provide specific risk control measures that can be implemented and verified by the manufacturer and that are considered to be effective in reducing the risk.
6.4 Residual risk evaluation	The limits defined in the standard typically mirror the generally accepted state of the art in risk control.	May provide methods or procedures on how to evaluate and determine the acceptability of risk (see Clause 5 Risk evaluation).
9 Production and post-production information	May provide specific requirements for mechanisms for the collection of production and post-production information.	May provide procedures for the selection and evaluation of post-production information, and for consecutive corrective actions.

Annex A (informative)

Product and process safety standards

A.1 Product standards

In general, for product standards to contribute to the safety and the effectiveness of medical devices, they need to be based on scientific data derived from laboratory or clinical studies, using state-of-the-art scientific methods such as statistical techniques, and peer review or best practice as used in medical devices of the same or similar type.

Product standards use a variety of sound engineering methods intended to manage risk to an acceptable level. Examples include the following:

- generally accepted state-of-the-art safety limits for physical, chemical or biological impact on human beings (X-ray dose, electrical current limits, surface temperature limits, bio-burden limits, leachable substance limits);
- standardized environmental conditions (temperature and humidity ranges, electromagnetic fields, specially controlled operating environments);
- standardized human interfaces (indicators, colours, symbols, alarm concepts, documentation requirements);
- generally accepted state-of-the-art constructional details (electrical insulation, cable connections);
- standardized tests to demonstrate conformance (EMC testing, conductive test finger, biocompatibility tests).

A.2 Process standards

While it is accepted that process standards can contribute to safety and effectiveness, it is generally more difficult to quantify the extent of the contribution. However, they can represent the generally accepted state-of-the-art practice, mainly focussing on those aspects that achieve an intended outcome (e.g. meeting a safety specification) in a controlled way. Process standards also contribute to ensuring that product standards are consistently implemented.

Process standards may contribute to the safety of medical devices, by the standardization of processes that are essential for the creation of safe medical devices, including processes to control design, validation, manufacture, and service. Although not specifically written for risk management purposes, the following are examples of process standards that facilitate risk management.

- state-of-the-art document control, which is a prerequisite for any product creation process; this is typically covered by quality management system standards (e.g. ISO 13485);
- agreed framework for selecting biological tests (e.g. the ISO 10993 series) and agreed methods for the sterilization processes for medical devices (e.g. ISO 11135-1 or ISO 11137-1).

Annex B **(informative)**

Risk information

Writers of standards should provide sources or methods for obtaining risk information, for example with regard to harm that could result from certain hazards, the probability of occurrence of harm as a result of a hazardous situation, or reliability data that may relate to the relevant risks. Such information may be obtained from external sources or internal experimentation (Data Collection and Analysis).

Possible data sources for risk information are the following:

- systematic review of peer-reviewed literature using medical and paramedical databases;
- technical papers from relevant standards committees;
- literature such as theses and internal industry documentation;
- other unpublished sources known to experts in the field;
- raw data from published trials;
- competent authority databases;
- reliability data bases;
- references in other standards;
- non-peer-reviewed journals and unverified Internet sources.

Discretion should be exercised when choosing information sources.

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