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Medical devices — Risk management —

Part 1:
Application of risk analysis

Dispositifs médicaux — Gestion du risque —

Partie 1: Application de l'analyse du risque

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Contents

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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.

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.

International Standard ISO 14971-1 was prepared jointly by Technical Committee ISO/TC 210, *Quality management and corresponding general aspects for medical devices*, and IEC/SC 62A, *Common aspects of electrical equipment in medical practice*.

ISO 14971 consists on the following parts, under the general title *Medical devices — Risk management*:

— *Part 1: Application of risk analysis*

Annexes A to F of this part of ISO 14971 are for information only.

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Introduction

Judgements relating to safety, including the acceptability of risks, are necessary in order to determine the suitability of a medical device for its intended use. Factors influencing the perception of safety include the socio-economic and educational background of the society concerned, and the actual and projected situation and status of the patient. Such judgements must take into account the intended use, performance, risks and benefits of the device, and the risks and benefits associated with the clinical procedure.

The overall process for the control of risks is referred to as "risk management". This part of ISO 14971 describes techniques for risk analysis based on quantitative or qualitative estimation of the probability of possible consequences of a postulated event relating to the application of a medical device. Risk analysis is the initial step in the overall process referred to as risk management. Elements of risk evaluation and risk control are included in the flow diagram (figure 1) for purposes of completeness. The relationship between risk analysis, risk evaluation and risk control is illustrated in annex E. Further work is under consideration.

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Medical devices — Risk management

Part 1:
Application of risk analysis

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1 Scope

This part of ISO 14971 specifies a procedure for investigating, using available information, the safety of a medical device, including *in vitro* diagnostic devices (IVD) or accessories, by identifying hazards and estimating the risks associated with the device. It may be of particular assistance in areas where relevant standards are not available or not used.

This part of ISO 14971 does not stipulate levels of acceptability because these are determined by a multiplicity of factors that cannot be set down in such a standard.

This part of ISO 14971 is not intended to give guidance on all aspects of management of risks. Furthermore, it is not intended to cover decision-making processes regarding assessment of the indications and contra-indications for the use of a particular device.

2 Definitions

For the purposes of this part of ISO 14971, the following definitions apply.

2.1
harm
physical injury and/or damage to health or property
[ISO/IEC Guide 51]

2.2
hazard
potential source of harm
[ISO/IEC Guide 51]

2.3
risk
probable rate of occurrence of a hazard causing harm and the degree of severity of the harm
[ISO/IEC Guide 51]

2.4
risk analysis
investigation of available information to identify hazards and to estimate risks

NOTE 1 See annex E.

NOTE 2 Examples of sources of information are given in note 3 in subclause 3.4.

2.5
safety
freedom from unacceptable risk of harm
[ISO/IEC Guide 51]

3 Procedure

3.1 General

The risk analysis procedure described in 3.2 to 3.9 and illustrated in the flow diagram given in figure 1 shall be followed. A record of the conduct and results of the risk analysis procedure shall be documented and maintained by the manufacturer.

NOTE 1 Risk analysis can be carried out as part of a quality system.

NOTE 2 The documentation of the conduct and results of the risk analysis procedure should include at least the following:

a) a complete description and identification of the device or accessory under consideration;

b) a list of possible hazards as identified under 3.3;

c) an indication of the methods by which risks have been reduced to acceptable levels;

d) identification of which party carried out the risk analysis.

3.2 Identification of qualitative and quantitative characteristics related to medical devices

For the particular device or accessory being considered, all those characteristics that could affect its safety and, where appropriate, their defined limits should be listed.

NOTE 1 Additional guidance on risk analysis techniques for IVDs is given in annex A.

NOTE 2 Additional guidance on risk analysis techniques for toxicological hazards is given in annex B.

The following questions can serve as a useful guide in drawing up such a list.

a) What is the intended use and how is the device to be used?

Factors that should be considered include the intended user, the required skill and training of the user, ergonomic aspects, the environment(s) 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 device. Special attention should be paid to 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 device.

b) Is the device intended to come into contact with the patient or other persons?

Factors that should be considered include intended contact, surface contact, invasive contact, implantation and, respectively, period and frequency of contact.

c) What materials and/or components are incorporated in the device or are used?

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

d) 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 time function.

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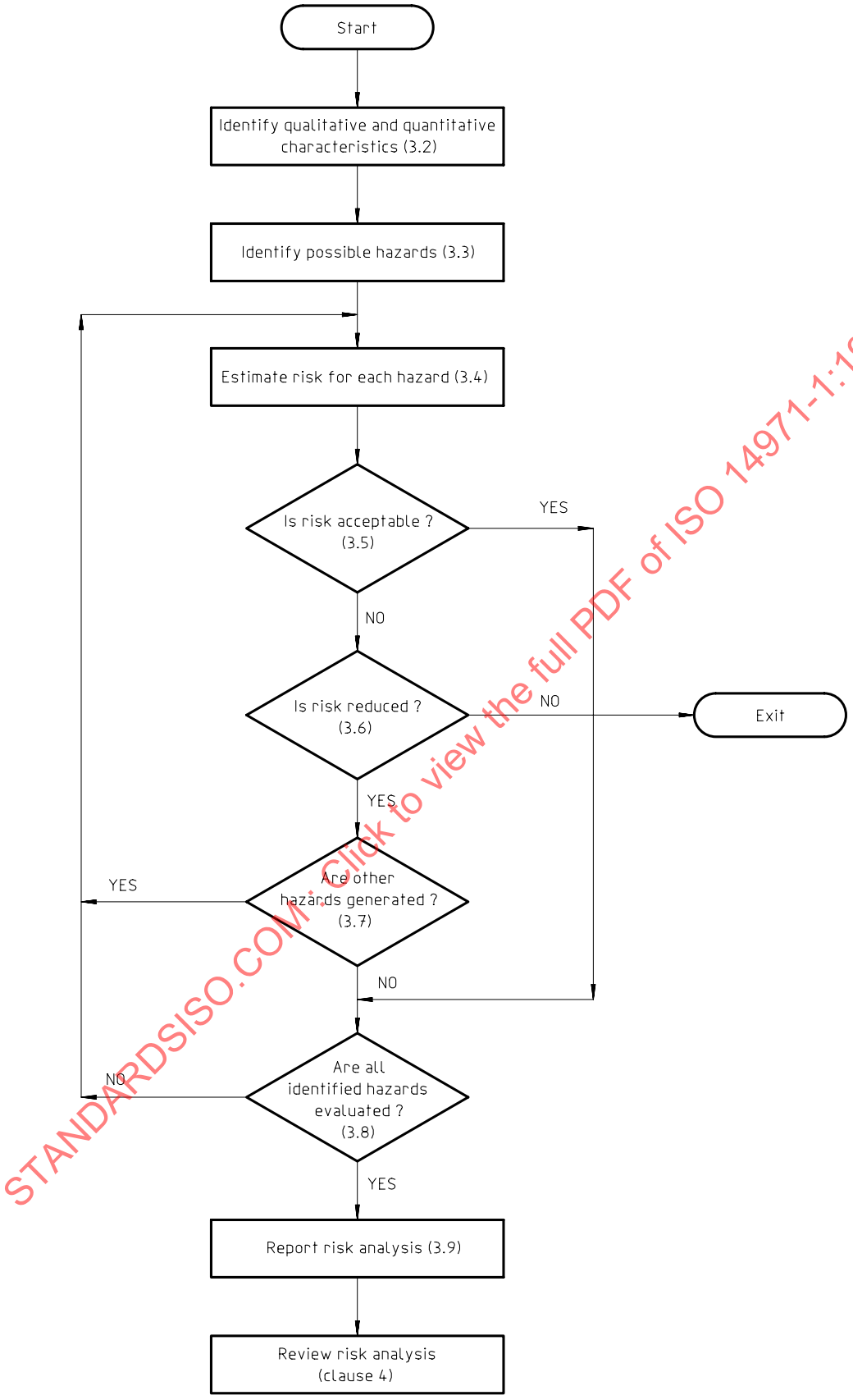

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Figure 1 — Flow diagram of risk analysis procedure

e) 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.

f) Are biological materials processed by the device for subsequent re-use?

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

g) Is the 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 device is intended for single-use or to be re-usable, any packaging, the shelf-life and any limitation on the number of re-use cycles, or type of sterilization process to be used.

h) Is the device intended to modify the patient environment?

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

i) Are measurements made?

Factors that should be considered include the variables measured and the accuracy and the precision thereof.

j) Is the device interpretative?

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

k) Is the device intended to control or to interact with other devices or drugs?

Factors that should be considered include identifying other devices and drugs which can be involved and the potential problems associated with such interactions.

l) 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 electrical and/or magnetic fields.

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

m) Is the device susceptible to environmental influences?

Factors that should be considered include the operational, transport and storage environment, including spillage, and power and cooling supplies.

n) Are there essential consumables or accessories associated with the device?

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

o) 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.

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p) Does the device contain software?

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

q) Does the device have a restricted "shelf-life"?

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

r) Possible delayed and/or long-term use effects?

Factors that should be considered include ergonomic and cumulative effects.

s) To what mechanical forces will the device be subjected?

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

t) What determines the lifetime of the device?

Factors that should be considered include ageing and battery depletion.

u) Is the device intended for single use or re-use?

3.3 Identification of possible hazards

Using the examples of possible hazards listed in annex C and in A.2 for IVDs as an *aide-mémoire*, compile a list of potential hazards associated with the device under both normal and fault conditions.

3.4 Estimation of the risks for each hazard

For each of the possible hazards identified under 3.3, the risks under both normal and fault conditions shall be estimated using available information/data. 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, in order to produce a measure of the level of the risks being analysed.

NOTE 1 In order to analyse risks, their components (i.e. consequences and probability) should be analysed separately. This may be done by quantitative or qualitative methods as appropriate. This includes answering the following questions:

— does the hazard exist in the absence of a failure?
— does the hazard exist in a failure mode?
— does the hazard exist only in a multiple fault condition?

Annex D and annex A.3 for IVDs give information on some risk analysis techniques that can be used.

NOTE 2 Techniques that can be used for the analysis of the risks include Failure Mode Effect Analysis (FMEA), Fault Tree Analysis (FTA) and Hazard and Operability (HAZOP) studies. The need for, selection of, and use of such techniques can depend on the nature of the device and are outside the scope of this part of ISO 14971.

Annex D gives a short summary of some of the techniques that can be used. IEC 60300-3-9 gives more details on these concepts. Annex F is a bibliography.

NOTE 3 Information/data can be obtained, for example, from:

— relevant standards;
— scientific data;
— field data from similar devices already in use, including published reported incidents;

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— clinical evidence;
— results of appropriate investigations.

3.5 Review of risks

If a risk for a given hazard is appropriately addressed by compliance with a relevant standard, or acceptability is demonstrated by other means, proceed to 3.8. If the risk for a given hazard estimated in accordance with 3.4 exceeds the levels of acceptability defined through the application of relevant standards or by other means, proceed to 3.6.

If the risk is judged to be outside acceptable limits only in failure mode, the likelihood of a fault occurring should be analysed. In doing this, the following questions should be addressed:

— can a failure be detected by the user before the hazard occurs?
— could the failure be eliminated by more effective manufacturing controls or by preventive maintenance?
— will misuse increase the likelihood of failure?
— can alarms be added?

3.6 Risk reduction

If the risk is reduced appropriately, proceed to 3.7. If the risk is not reduced appropriately, exit the analysis procedure.

Risks can be reduced to acceptable levels by appropriate means, such as:

a) direct safety means (design);

b) indirect safety means (safeguarding); examples of safeguarding are:
   — restricting accessibility (e.g. for radiation hazards),
   — shielding from the hazard (e.g. by means of a protective cover);

c) descriptive safety means (e.g. restricting period or frequency of use of the device, restricting application, lifetime, or environment);

d) redefining the intended use.

3.7 Generation of other hazards

Determine whether the risk reduction procedure has introduced new hazards.

3.8 Evaluation of all identified hazards

If risks have been estimated for all identified hazards, proceed to 3.9, if not, return to 3.4.

NOTE Where third-party verification is not used, analysis verification as in subclause 5.5 of IEC 60300-3-9:1995 may be followed.

3.9 Risk analysis report

Document the results of the risk analysis according to 3.1 so that a decision can be taken as to whether the remaining risks associated with the identified hazards are acceptable, having regard to the intended application and use of the device.

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4 Review of risk analysis

When new information/data becomes available, a new risk analysis should be considered.

NOTE A review of the risk analysis may be necessary if risks change over time. Rapidly changing technology can eliminate, increase or decrease the risk for any given hazard. New risks can arise or be identified for the first time.

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Annex A
(informative)

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

A.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 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 device-associated hazards leading or contributing to erroneous decisions. In addition, user-related hazards and their associated risks should be considered.

A.2 Identification of hazards

In addition to those aspects mentioned in annex C, 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;

— sample 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.

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).

A.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.

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Annex B
(informative)

Guidance on risk analysis procedure for toxicological hazards

B.1 General

This annex provides guidance on the procedure to be followed in the risk analysis procedure 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/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 legislation, e.g. the European Community Directive on Animal Protection (86/609/EEC).

A test may be omitted if the omission can be scientifically justified.

B.2 Estimation of toxicological risks

B.2.1 General

The toxicological risk analysis should take account of:

— the chemical nature of the materials;

— prior use of the materials;

— biological safety test data.

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

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

B.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. Some factors which 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, etc.);

— 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.

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

B.2.3 Prior use

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

B.2.4 Biological safety test data

ISO 10993-1 gives guidance on which tests should be considered for particular applications. 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.

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Annex C
(informative)

Examples of possible hazards and contributing factors associated with medical devices

C.1 General

Clauses C.2 to C.7 give non-exhaustive lists of possible hazards and contributing factors associated with different medical devices. These lists are intended to provide an *aide-mémoire* in identifying possible hazards given in 3.3 of the risk analysis procedure (step 3 of figure 1).

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C.2 Energy hazards

These include the following:

— electricity
— heat
— mechanical force
— ionizing radiation
— non-ionizing radiation
— electromagnetic fields
— moving parts
— suspended masses
— patient support device failure
— pressure (vessel rupture)
— acoustic pressure
— vibration
— magnetic fields (e.g. MRI)

C.3 Biological hazards

These include the following:

— bio-contamination
— bio-incompatibility
— incorrect output (substance/energy)
— incorrect formulation (chemical composition)
— toxicity
— allergenicity
— mutagenicity

— teratogenicity
— carcinogenicity
— (cross-)infection
— pyrogenicity
— inability to maintain hygienic safety
— degradation

C.4 Environmental hazards

These include the following:

— electromagnetic interference
— inadequate supply of power or coolant
— restriction of cooling
— likelihood of operation outside prescribed environmental conditions
— incompatibility with other devices
— accidental mechanical damage
— contamination due to waste products and/or device disposal

C.5 Hazards related to the use of the device

These include the following:

— inadequate labelling
— inadequate operating instructions
— inadequate specification of accessories
— inadequate specification of pre-use checks
— over-complicated operating instructions
— unavailable or separated operating instructions
— use by unskilled/untrained personnel
— reasonably foreseeable misuse
— insufficient warning of side effects
— inadequate warning of hazards likely with re-use of single-use devices
— incorrect measurement and other metrological aspects
— incorrect diagnosis
— erroneous data transfer
— mispresentation of results
— incompatibility with consumables/accessories/other devices

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C.6 Hazards arising from functional failure, maintenance and ageing

These include the following:

— inadequacy of performance characteristics for the intended use

— lack of, or inadequate specification for, maintenance, including inadequate specification of post-maintenance functional checks

— inadequate maintenance

— lack of adequate determination of end of device life

— loss of mechanical integrity

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

— improper re-use

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