TECHNICAL REPORT

ISO/TR 24971

Redline version compares Second edition to First edition

Medical devices — Guidance on the application of ISO 14971

Dispositifs médicaux — Recommandations relatives à l'application de l'ISO 14971

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Text example 1 — Text has been added (in green)

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 — Graphic figure has been added

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1.x ... — If there are changes in a clause/subclause, the corresponding clause/subclause number is highlighted in yellow in the Table of contents

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This marked-up version highlights the main changes in this edition of the document compared with the previous edition. It does not focus on details (e.g. changes in punctuation).

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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.

The *procedures* used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2~~.~~ (see ~~www.iso.org/directives~~www.iso.org/directives-and-policies).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received~~.~~ (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see the following URL: www.iso.org/iso/foreword.html.

~~ISO/TR 24971~~This document was prepared jointly by Technical Committee ISO/TC 210, *Quality management and corresponding general aspects for medical devices*, and ~~Technical Committee~~Subcommittee IEC/SC 62A, *Common aspects of electrical equipment used in medical practice*. ~~The draft was circulated for voting to the national bodies of both ISO and IEC.~~

This second edition cancels and replaces the first edition, which has been technically revised. The main changes compared to the previous edition are as follows:

— The clauses of ISO/TR 24971:2013 and some informative annexes of ISO 14971:2007 are merged, restructured, technically revised, and supplemented with additional guidance.

— To facilitate the use of this document, the same structure and numbering of clauses and subclauses as in ISO 14971:2019 is employed. The informative annexes contain additional guidance on specific aspects of *risk management*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

~~Experience indicates that~~This document provides guidance to assist *manufacturers* ~~have difficulty with practical implementation of some clauses of the~~ in the development, implementation and maintenance of a *risk management* ~~*International Standard*~~, *process* for *medical devices* that aims to meet the requirements of ISO 14971:~~2007~~2019, *Medical devices — Application of risk management to medical devices*. ~~This Technical Report provides guidance to assist in the development, implementation and maintenance of risk management for medical devices that aim to meet the requirements of~~ It provides guidance on the application of ISO 14971:2019~~. It provides guidance for specific aspects of for ISO 14971~~ for a wide variety of *medical devices*. These *medical devices* include active, non-active, implantable, and non-implantable *medical devices*, software as *medical devices* and *in vitro diagnostic medical devices*.

~~This Technical Report is not intended to be an overall guidance document on the implementation~~The clauses and subclauses in this document have the same structure and numbering as the clauses and subclauses of ISO 14971:2019 ~~for organizations. It supplements the guidance contained in the informative annexes~~, to facilitate the use of this guidance in applying the requirements of the standard. Further division into subclauses is applied where considered useful. The informative annexes contain additional guidance on specific aspects of *risk management*. The guidance consists of the clauses of ISO ~~14971~~/TR 24971:2013 ~~related to the following areas~~and some of the informative annexes of ISO 14971:2007, which are merged, restructured, technically revised, and supplemented with additional guidance.

- ~~Guidance on the role of international product safety and process standards in risk management~~
- ~~Guidance on developing the policy for determining the criteria for risk acceptability~~
- ~~Guidance on how the production and post-production feedback loop can work~~
- ~~Guidance on the differentiation of information for safety as a risk control measure and disclosure of residual risk~~
- ~~Guidance on the evaluation of overall residual risk~~

Annex H was prepared in cooperation with Technical Committee ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems*.

This ~~Technical Report provides some~~document describes approaches that *manufacturers*~~an organization~~ can use to develop, implement and maintain ~~some aspects of~~ a *risk management process* ~~system that conforms~~conforming to ISO 14971:2019. Alternative approaches can ~~be used if these~~also satisfy the requirements of ISO 14971:2019.

When judging the applicability of the guidance in this ~~Technical Report~~document, one should consider the nature of the *medical device(s)* to which it will apply, ~~the risks associated with the use of~~how and by whom these *medical devices* are used, and the applicable regulatory requirements.

Medical devices — Guidance on the application of ISO 14971

1 Scope

This ~~Technical Report provides guidance in addressing specific areas~~document provides guidance on the development, implementation and maintenance of ~~ISO 14971 when implementing risk management~~a *risk management* system for *medical devices* according to ISO 14971:2019.

The *risk management process*~~guidance is intended~~ can be part of a quality management system, for example one that is based on ISO 13485:2016[24], but this is not required by ISO 14971:2019. Some requirements in ISO 13485:2016 (Clause 7 on product realization and 8.2.1 on feedback during monitoring and measurement) are related to *risk management*~~assist manufacturers and other users of~~ and ~~the standard to~~can be fulfilled by applying ISO 14971:2019. See also the ISO Handbook: *ISO 13485:2016 — Medical devices — A practical guide*[25].

~~— understand the role of international product safety and process standards in risk management;~~

~~— develop the policy for determining the criteria for risk acceptability;~~

~~— incorporate production and post-production feedback loop into risk management;~~

~~— differentiate between "information for safety" and "disclosure of residual risk"; and~~

~~— evaluate overall residual risk.~~

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 14971:2019, *Medical devices — Application of risk management to medical devices*

~~2~~3 ~~The role of international product safety and process standards in risk management~~Terms and definitions

~~2.1 Overview~~

~~International product safety and process standards play a significant role in risk management as described by ISO 14971. In principle, these standards are developed using a type of risk management that can include identifying hazards and hazardous situations, estimating risks, evaluating risks, and specifying risk control measures. More information on a process for developing medical device standards using a type of risk management can be found in documents such as ISO/IEC Guide 51 and ISO/IEC Guide 63. International product safety and process standards are developed by experts in the field and represent the generally accepted state of the art (see D.4 of ISO 14971:2007).~~

~~These standards can have an important role in risk management. When performing risk management, the manufacturer first needs to consider the medical device being designed, its intended use and the hazards/hazardous situations related to it. Manufacturers can, if they choose, identify standard(s) that contain specific requirements that help manage the risks related to those hazards/hazardous situations.~~

~~For medical devices that satisfy the requirements and compliance criteria of these standards, the residual risks related to those hazards/hazardous situations can be considered acceptable unless there~~

is objective evidence to the contrary. Some potential sources of objective evidence to the contrary can include reports of adverse events, product recalls and complaints. The requirements of International Standards, such as engineering or analytical processes, specific output limits, warning statements, or design specifications, can be considered risk control measures established by the standards writers that are intended to address the risks of specific hazardous situations that have been identified and evaluated as needing risk control.

In many cases, the standards writers have taken on and completed elements of risk management and provided manufacturers with answers in the form of design requirements and test methods for establishing conformity. When performing risk management activities, manufacturers can take advantage of the work of the standards writers and need not repeat the analyses leading to the requirements of the standard. International standards, therefore, provide valuable information on risk acceptability that has been validated during a worldwide evaluation process, including multiple rounds of review, comment, and voting.

2.2 Use of international product safety standards in risk management

An international product safety standard can establish requirements that, when implemented, result in acceptable risk for specific hazardous situations (e.g. safety limits). The manufacturer can apply these requirements in the following way when managing risk:

a) Where an international product safety standard specifies technical requirements addressing particular hazards or hazardous situations, together with specific acceptance criteria, compliance with those requirements is presumed to establish that the residual risks have been reduced to acceptable levels unless there is objective evidence to the contrary. For example, in IEC 60601-1, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*, leakage current must be controlled to achieve an acceptable level of risk. IEC 60601-1 provides leakage current limits that are considered to result in an acceptable level of risk when measured under the conditions stated in 8.7 of IEC 60601-1:2005. For this example, further risk management would not be necessary. The following steps need to be taken in this case.

   1) Implement 4.2 and 4.3 of ISO 14971:2007 to identify characteristics related to safety and identify hazards and hazardous situations associated with the device as completely as possible.

   2) Identify those hazards and hazardous situations relevant to the particular medical device that are exactly covered by the international product safety standard.

   3) For those identified hazards and hazardous situations exactly covered by the international product safety standard, the manufacturer may choose not to estimate (4.4 of ISO 14971:2007) or evaluate (Clause 5 of ISO 14971:2007) the risks so identified but rather rely on the requirements contained in the international standard to demonstrate the completion of risk estimation and risk evaluation.

   4) To the extent possible, the manufacturer should identify the design specifications that satisfy the requirements in the standard and serve as risk control measures (6.2 of ISO 14971:2007).

      NOTE For some international product safety standards, the possibility of identifying all the specific risk control measures is limited. One example is electromagnetic compatibility testing in IEC 60601-1-2, *Medical electrical equipment — Part 1-2: General requirements for basic safety and essential performance — Collateral standard: Electromagnetic compatibility — Requirements and tests*, for complex medical devices.

   5) Verification of the implementation of the risk control measures for these hazardous situations is obtained from the design documents. Verification of the effectiveness of the risk control measures is obtained from the tests and test results demonstrating that the device meets the relevant requirements of the international product safety standard.

   6) If the relevant requirements are met, the associated residual risk is considered acceptable.

b) Where an international product safety standard does not completely specify technical requirements and associated tests and test acceptance criteria, the situation is more complex. In some cases, the

standard directs the manufacturer to perform specific tests related to known hazards or hazardous situations but does not provide specific test acceptance criteria (e.g. IEC 60601-2-16, *Medical electrical equipment — Part 2-16: Particular requirements for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment*). In some other cases, the standard can simply direct the manufacturer to investigate specific hazards or hazardous situations in their risk analysis (e.g. 10.2 of IEC 60601-1:2005). The range of alternatives is too large to provide specific guidance on how to use such standards in the risk management process. Manufacturers are encouraged, however, to use the content of such standards in their risk management of the particular medical device.

c) For hazards or hazardous situations that are identified for the particular medical device but are not specifically addressed in any standard, the manufacturer needs to address those hazards or hazardous situations in the risk management process. The manufacturer is required to estimate and evaluate the risks and, if necessary, control these risks (see 4.4 and Clauses 5 and 6 of ISO 14971:2007).

See Figure 1 for a flowchart and an example outlining the use of international product safety standards.

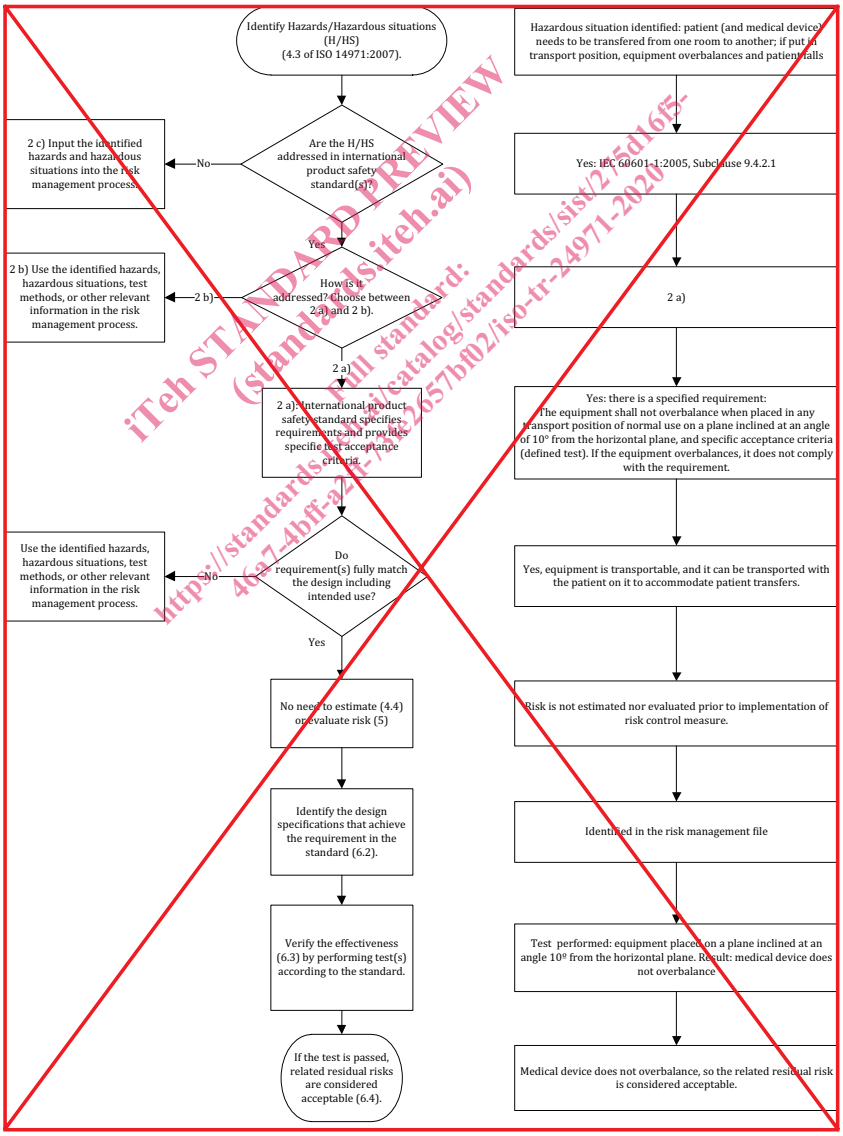

Figure 1 — Use of international product safety standards and example of such standard that specifies requirements and provides specific test acceptance criteria

2.3 International process standards and ISO 14971

International process standards, as shown in the examples below, can often be used in conjunction with ISO 14971. This is performed in one of two ways:

- The international process standard requires application of ISO 14971 as part of the implementation of the international process standard, e.g. IEC 62304 on software life cycle processes; or
- The international process standard is intended to be used in risk management, e.g. IEC 62366 on usability engineering and the ISO 10993 series on biological evaluation.

In either case, proper use of the international process standard requires attention to the interfaces between that standard and ISO 14971 in order to achieve acceptable levels of risk for the medical device. The two standards should work together such that inputs, outputs and their timing are optimized. Three examples are given below to demonstrate this ideal situation.

a) IEC 62304, *Medical device software — Software life cycle processes*

The relationship between IEC 62304 and ISO 14971 is well-described in the introduction to IEC 62304.

As a basic foundation it is assumed that MEDICAL DEVICE SOFTWARE is developed and maintained within a quality management system (see 4.1 of IEC 62304:2006) and a RISK MANAGEMENT process (see 4.2 of IEC 62304:2006). The RISK MANAGEMENT PROCESS is already very well addressed by the International Standard ISO 14971. Therefore IEC 62304 makes use of this advantage simply by a normative reference to ISO 14971. Some minor additional RISK MANAGEMENT requirements are needed for software, especially in the area of identification of contributing software factors related to HAZARDS. These requirements are summarized and captured in Clause 7 of IEC 62304:2006 as the software RISK MANAGEMENT PROCESS.

Whether software is a contributing factor to a HAZARD is determined during the HAZARD identification ACTIVITY of the RISK MANAGEMENT PROCESS. HAZARDS that could be indirectly caused by software (for example, by providing misleading information that could cause inappropriate treatment to be administered) need to be considered when determining whether software is a contributing factor. The decision to use software to control RISK is made during the RISK CONTROL ACTIVITY of the RISK MANAGEMENT PROCESS. The software RISK MANAGEMENT PROCESS required in this standard has to be embedded in the device RISK MANAGEMENT PROCESS according to ISO 14971.

IEC 62304 makes a normative reference to ISO 14971 and specifically requires:

- software development planning (5.1 of IEC 62304:2006) that is consistent with the risk management plan required by ISO 14971, and
- a software risk management process (Clause 7 of IEC 62304:2006) based upon ISO 14971.

b) IEC 62366, *Medical devices — Application of usability engineering to medical devices*

The flow diagram in Figure A.1 of IEC 62366:2007 demonstrates the relationship and interconnection of the two parallel and interconnecting processes. In addition to making a normative reference to ISO 14971, IEC 62366:2007 identifies three specific clauses where the usability engineering process can supplement and interact with risk management as described in ISO 14971.

- 5.3.1 of IEC 62366:2007 requires: "An identification of characteristics related to SAFETY (part of a RISK ANALYSIS) that focuses on USABILITY shall be performed according to ISO 14971:2007, 4.2."
- 5.3.2 of IEC 62366:2007 requires: "The MANUFACTURER shall identify known or foreseeable HAZARDS (part of a RISK ANALYSIS) related to USABILITY according to ISO 14971:2007, 4.3."
- 5.9 of IEC 62366:2007 on Usability Validation makes several references to activities that would be undertaken as part of risk management.

c) ISO 10993 (all parts), *Biological evaluation of medical devices*

The introduction to ISO 10993-1 states that ISO 10993-1 is intended to be a guidance document for the biological evaluation of medical devices within risk management, as part of the overall evaluation and development of each device.

Annex B of ISO 10993-1:2009 applies ISO 14971 to provide guidance on the risk management approach for identification of biological hazards associated with medical devices, estimation and evaluation of the risks, control of the risks, and monitoring the effectiveness of the risk control measures.

This approach combines the review and evaluation of existing data from all sources, with the selection and application of additional tests (where necessary), thus enabling a full evaluation to be made of the biological responses to each medical device, relevant to its safety in use.

ISO 10993-1:2009 aligns itself explicitly within risk management as described in ISO 14971.

The biological evaluation should be conducted in a manner similar to that used for other product risks, and should include:

— Risk analysis (What are the hazards and associated risks?)

— Risk evaluation (Are they acceptable?)

— Risk control (How will they be controlled?)

— Overall residual risk/benefit evaluation

Following the processes defined in ISO 14971, if the overall residual risk evaluation concludes from existing data that the identified risks are acceptable, no further risk control is needed. Otherwise, appropriate measures should be taken to further evaluate or mitigate the risks.

The output of this evaluation is a Biological Evaluation Report.

Application

— Conditions identified as hazards in ISO 10993-1 include:

  — Acute toxicity

  — Chronic toxicity

  — Irritation (skin, eye, mucosal surfaces)

  — Hypersensitivity

  — Genotoxicity

  — Carcinogenicity

— Do the proposed materials in the particular medical device cause such conditions?

— Methods that are used to determine if a material in the particular medical device can result in the conditions listed above include:

  — Chemical characterization and assessment

  — Literature review

  — Testing (*in vitro*/*in vivo*, non-clinical)

  — Field experience

— Are the exposure levels acceptable?

According to ISO 10993-1, expert assessors should determine if the available information/data are sufficient to determine if the overall residual risk associated with biological hazards is acceptable. This conclusion is documented in the Biological Evaluation Report, which becomes an element of the risk management file.

For the purposes of this document, the terms and definitions given in ISO 14971:2019 apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

NOTE The defined terms in ISO 14971:2019 are derived as much as possible from ISO/IEC Guide 63:2019[20] which was developed specifically for the *medical device* sector.

3 4 Developing the policy for determining the criteria for General requirements for *risk acceptability management* system

According to 3.2 of ISO 14971:2007, top management is required to define and document the policy for determining the criteria for risk acceptability. This policy is intended to ensure that criteria:

a) are based upon applicable national or regional regulations;

b) are based upon relevant International Standards;

c) take into account available information such as the generally accepted state of the art and known stakeholder concerns.

NOTE Other relevant information can also be included.

The policy could cover the entire range of a manufacturer's medical devices or it can take different forms depending on whether the medical devices are similar to each other, or whether the differences between groups of medical devices are significant.

When developing or maintaining the policy the following should be taken into consideration:

— The applicable regulatory requirements in the regions where the medical device is to be marketed.

— The relevant International Standards for the particular medical device or an intended use of the medical device that can help identify principles for setting the criteria for risk acceptability (see 2.2).

— Information on the state of the art can be obtained from review of the literature and other information on similar medical devices the manufacturer has marketed, as well as those from competing companies.

— The validated and comprehensive concerns from the main stakeholders. Some potential sources of information on the patient and clinician perspective can include news media, social media, patient forums, as well as input from internal departments with expert knowledge of stakeholder concerns such as the clinical department.

The manufacturer should provide guidelines for developing the actual criteria for risk acceptability to be used in the risk management plan for the particular medical device being considered (see 3.4 of ISO 14971:2007).

The review of the suitability of the risk management process at planned intervals, as required by 3.2 of ISO 14971:2007, can demonstrate the appropriateness of previously used criteria for risk acceptability or lead to changes in the policy. Such changes can also lead to reviewing the appropriateness of previous risk acceptability decisions.

4.1 *Risk management process*

ISO 14971:2019 requires that the *manufacturer* establishes, implements, documents and maintains an ongoing *risk management process* throughout the *life cycle* of the *medical device*. The required elements in this *process* and the responsibilities of *top management* are given in ISO 14971:2019 and explained in further detail in this document.

4.2 Management responsibilities

4.2.1 *Top management* commitment

Top management has the responsibility to establish and maintain an effective *risk management process*. It is important to note the emphasis on *top management* in ISO 14971:2019 *Top management* has the power to assign authorities and responsibilities, to set priorities and to provide resources within the organization. Commitment at the highest level of the organization is essential for the *risk management process* to be effective.

If the *manufacturer's* organization consists of separate entities, for example business units or divisions, then *top management* can refer to those individuals who direct and control the entity implementing the *risk management process*. Each entity can have its own *risk management process* (and its own quality management system).

4.2.2 Policy for establishing criteria for *risk* acceptability

ISO 14971:2019 requires *top management* to define and document the policy for establishing criteria for *risk* acceptability. Annex C provides detailed guidance on how to define such a policy and which elements should be included, such as applicable regulations, relevant international standards, the generally acknowledged *state of the art* and known stakeholder concerns. Annex C also explains the relation between the policy and the criteria for *risk* acceptability and how these criteria are used in *risk control* and *risk evaluation*.

The policy can allow specific criteria for each type of *medical device* (or *medical device* family). This can depend on the characteristics of the *medical device* and its *intended use* (including the intended patient population). ISO 14971:2019 requires that the policy provides guidelines on how to establish the criteria for acceptability of the overall *residual risk*.

4.2.3 Suitability of the *risk management process*

ISO 14971:2019 requires *top management* to review the suitability of the *risk management process* at planned intervals. The review of the suitability is a high-level review of the *risk management process* and can include reviewing the following aspects, for example:

— the effectiveness of the implemented *risk management procedures*;

— the adequacy of the criteria for *risk* acceptability, which can imply the need for an adaptation of the criteria for *risk* acceptability for specific *medical devices*; and

— the effectiveness of the feedback loop of the production and *post-production* information (see 10.4).

4.3 Competence of personnel

Ensuring the assignment of competent personnel is a responsibility of *top management*. Examples of the personnel that can be involved in specific *risk management* tasks and the relevant knowledge and experience supporting effective completion of the associated tasks are given in Table 1.

Some *risk management* activities can be performed by external consultants or specialists. The required competence should be documented as well as the *objective evidence* of the fulfilment of these requirements.