Notified Bodies Recommendation Group

Consensus Paper
for the
Interpretation and Application of
Annexes Z in
EN ISO 14971: 2012

Version 1.1

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Note : This document is for guidance only, please note that this document has not been accepted by the EU Commission and therefore is not a formal approved document.

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1.) Introduction

In October 2010, the regular review of ISO 14971:2007 which is the basis of EN ISO 14971:2009 was closed by a broad majority of votes confirming the existing status and the wide-spread acceptance of this standard in the medical devices community, including competent authorities. In November 2010, the European Commission raised a formal objection against the use of several harmonized standards, including EN ISO 14971, followed by an in-depth assessment of the coverage of the Essential Requirements of the Medical Device Directives (90/385/EEC, 93/42/EEC and 98/79/EC) by these standards.

As a result of these objections, the Annexes Z to EN ISO 14971 were modified, resulting in EN ISO 14971:2012. This amendment of the EN ISO 14971 standard did not modify the normative parts of ISO 14971:2007[1]. The Annexes Z describe the extent of presumption of conformity that can be based on application of the normative requirements of ISO 14971 alone. The “content deviations”, expressed in the revised Annexes Z, between ISO 14971:2007 and the Medical Device Directives have been commented by many experts in the field of risk management and resulted in diverging interpretations from different stakeholders (e.g. manufacturers, notified bodies, competent authorities).

This document has been prepared as a Notified Body Consensus Paper by a working group headed by the NBRG Vice Chair, with representatives from several European Notified Bodies and industry associations COCIR, Eucomed, EDMA and ZVEI. The paper aims to provide a practical interpretation of these “content deviations” to the Medical Device Directives and give guidance as to how to implement the risk management requirements. The work consolidates prior publications of various sources and is intended to facilitate common understanding between industry and Notified Bodies.

2.) Terminology

The three medical devices directives (93/42/EEC, 90/385/EEC and 98/79/EC) refer to “risk” and “safety” in a general sense. Since the time of writing these directives about 20 years ago, the knowledge of and experience in risk management have evolved considerably. This is reflected by the successive publication of EN1441 in 1994 and ISO14971-1 in 1998 as well as first (2000) and second (2007) editions of ISO 14971 which all have been recognized globally as the state of the art for risk management at the moment of their publication.

The wording of the risk management aspects in the essential requirements of the Medical Devices Directives has not been modified over time, however.

[1] EN ISO 14971:2012 Annexes Z apply to manufacturers placing devices on the market in the European Union; for the rest of the world, ISO 14971:2007 remains the applicable standard.

The international standard ISO 14971:2007 and its European equivalent EN ISO 14971:2012 contain specific defined terms with a clear and precisely described meaning. See Table 1 for an overview of the most relevant terms used in this document. Note that these defined terms are more precise than the general terms as used in the Medical Device Directive. For example, “risk” in the medical devices directives can bear the meaning of “risk”, “hazard” or “hazardous situation” depending on the context. This document is compiled on the assumption that “risk” in the Medical Device Directives is equivalent to “unacceptable risk” in ISO 14971:2007.

Term	Definition	Clause
Harm	Physical injury or damage to the health of people, or damage to property or the environment	(a) 2.2
Hazard	Potential source of harm	(a) 2.3
Hazardous situation	Circumstance in which people, property, or the environment are exposed to one or more hazard(s)	(a) 2.4
Risk	Combination of the probability of occurrence of harm and the severity of that harm	(a) 2.16
Risk control	process in which decisions are made and measures implemented by which risks are reduced to, or maintained within specified levels	(a) 2.19
Safety	Freedom from unacceptable risk	(a) 2.24
Disclosure of residual risks	Information in the accompanying documents on risks remaining after all risk control measures have been taken	(b) 5.1
Information for safety	Instructions of what actions to take or to avoid in order to prevent a hazardous situation from occurring	(b) 5.2

Table 1: Relevant terms from (a) ISO 14971:2007 and (b) ISO/TR 24971:2013

3.) General Considerations

This Consensus Paper intends to bridge the gap between the interpretation of the relevant Essential Requirements of the Medical Devices Directives, as given in the Annexes ZA, ZB, and ZC of EN ISO 14971:2012, and the practice of placing safe medical devices on the market in the EU and in other countries where the abovementioned directives apply. This chapter provides some considerations about risk management and how this is to be interpreted in the context of the European Medical Devices Directives.

The practical approach of this Consensus Paper safeguards the principle that only medical devices that are “compatible with a high level of protection of health and safety”[2] can be placed on the EU market. With this in mind, two aspects of the

[2] COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices.

European Commission's interpretation of EN ISO 14971:2012, as reflected in the Annexes Z, deserve further consideration:

1. Reduce risk "as far as possible", and
2. Economical considerations in Risk Management

1. Reducing risk "as far as possible"

The phrase "as far as possible" has led to significant confusion for those involved in placing medical devices on the market. Strict interpretation would create practical problems such as where to stop in reducing risk before a product can be placed on the market. This may restrict patient access to safe and affordable devices.

In line with Clause 1.1 of the 2013 edition of the European Commission, Parliament and Council's Joint Practical Guide of the European Parliament, the Council and the Commission for persons involved in the drafting of European Union legislation[3], this consensus paper offers Notified Bodies and manufacturers an interpretation of "as far as possible" that is "clear, easy to understand and unambiguous."

2. On economical considerations in Risk Management

"Content deviation" 3 in the Annexes Z of EN ISO 14971:2012 states:

> *a) Annex D.8 to ISO 14971, referred to in 3.4, contains the concept of reducing risks "as low as reasonably practicable" (ALARP concept). The ALARP concept contains an element of economic consideration.*
>
> *b) However, the* [Essential Requirements *require risks to be reduced "as far as possible" without there being room for economic considerations.*
>
> *c) Accordingly, manufacturers and Notified Bodies may not apply the ALARP concept with regard to economic considerations.*

This disregard of economic considerations when reducing risk is not coherent with the Medical Device Directives' objective as stated in, for example, the following recital[4] of Directive 93/42/EEC:

> Whereas the essential requirements and other requirements set out in the Annexes to this Directive, including any reference to 'minimizing' or 'reducing' risk must be interpreted and applied in such a way as to take account of technology and practice existing at the time of design and of technical **and economical considerations compatible with a high level of protection of health and safety**.

It should be noted that this specific recital on the relevance of economic considerations exists since the first publication of the original Directive.

[3] http://eur-lex.europa.eu/content/pdf/techleg/joint-practical-guide-2013-en.pdf

[4] Recitals are part of the legal text, as stated in Clause 10.1 of the Joint Practical Guide mentioned above and confirmed in the ECJ ruling C-219/11.

4.) Recommendations for Industry

The Annexes Z of EN ISO 14971:2012 list seven “content deviations”, i.e., differences between the wording of the Essential Requirements (ERs) in the Medical Device Directives and the wording of the requirements of the standard. Nevertheless, the Medical Device Directives and the standard share the same objectives of achieving a high level of product safety and ensuring continuous improvement. Parts of the content deviations are quoted and given here in *italics*. Specific recommendations for medical device manufacturers in relation to those “content deviations” are given below.

Content deviation 1: Treatment of negligible risks

“..the manufacturer must take all risks into account..”

Recommendation:

The manufacturer must identify known and foreseeable hazards and estimate the risk for each hazardous situation identified (Clause 4 of EN ISO 14971:2012). The risk control measures and the results of the risk evaluation must be recorded in the risk management file (Clause 5 and Clause 6.2 of EN ISO 14971:2012). This process ensures that all risks are given sufficient attention.

The manufacturer shall document all identified hazards and hazardous situations, their associated risks and the risk control measures for each individual risk, in the risk management file.

Compliance may be demonstrated by review of the risk management file.

Content deviation 2: Discretionary power of manufacturers as to acceptability of risks

“...all risks combined, regardless of any “acceptability assessment,” need to be balanced, together with all other risks, against the benefit of the device.”
“Accordingly, the manufacturer may not apply any criteria of risk acceptability prior to applying Sections 1 and 2 of Annex I to Directive 93/42/EEC (Sections 1 and 6 of Annex I to Directive 90/385/EEC respectively Sections A.1 and A.2 of Annex I to Directive 98/79/EC).”

Recommendation:

When determining the criteria for risk acceptability, the manufacturer shall consider whether death or serious deterioration of health is unlikely to occur in normal operation or due to device malfunctions or deterioration of characteristics or

performance, or any inadequacy in the labeling or instructions for use.[5] If unlikely to occur the risk shall be considered acceptable.
Otherwise, the risk must be reduced. In doing so, the manufacturer may choose an end-point for risk reduction, for example:

1.) The risk acceptability is preferably based on harmonized standards specifying state of the art risk control measures for particular categories of medical devices. Basing the risk reduction end-point on harmonized standards ensures that the risk is reduced to an acceptable level.

2.) If no harmonized standards are available, other national or international recognized standards or publications should be considered. Basing the risk reduction end-point on recognized international standards ensures that the risk is reduced to an acceptable level.

3.) Where those publications are not available, the manufacturer must assess the best risk reduction means and shall include in the description of the risk management process what criteria were used to determine the acceptability of risks. The criteria for risk acceptability are then based among others on historical data, best medical practice and state of the art.

4.) Further risk control measures do not improve the safety.

If a reduction to an acceptable level cannot be achieved, a risk-benefit analysis must demonstrate that the residual risk is outweighed by the medical benefit as explained in content deviation 4.

Compliance may be demonstrated by reflecting such end-points in the criteria for risk acceptability as part of the risk management file. Where safety cannot be demonstrated as such, existing clinical data is used to demonstrate that the medical benefit outweighs the risk.

<u>Content deviation 3:</u> Risk reduction "as far as possible" versus "as low as reasonably practicable"

"Essential requirements require risks to be reduced as far as possible without there being room for economic considerations..."

With this deviation the European Commission raises the concern that economic considerations might surmount safety considerations. On the other hand the reduction of a risk "as far as possible" could be without limits and the resulting devices might no longer be affordable for a larger group of patients.

Recommendation:

[5] coherent with criteria from Article 10 of Directive 93/42/EEC and corresponding requirements in Annexes (e.g. Annex II, 3.1) when deciding about Field Corrective Actions

Although economic considerations will always be relevant in decision-making processes, the safety of the product must not be traded off against business perspectives. For transparency the manufacturer must document the end-point criteria of risk reduction based on his risk policy.

Compliance is checked by inspection of the documentation

<u>Content deviation 4:</u> Discretion as to whether a risk-benefit analysis needs to take place

"the manufacturer must undertake a risk-benefit analysis for the individual risk and the overall risk-benefit…"

Recommendation:

At the end of the risk management process the manufacturer shall perform a riskbenefit analysis for individual risks that are not acceptable according to the criteria explained in content deviation 2 and for which further risk reduction is not possible. In any case the manufacturer shall perform an overall risk-benefit analysis considering all individual risks to provide a rationale for overall risk acceptance.

Compliance is checked by inspection of the individual and overall risk-benefit analyses.

<u>Content deviation 5:</u> Discretion as to the risk control options

"…the manufacturer must apply all the control options and may not stop his endeavors if the first or second control option has reduced the risk to an "acceptable" level (unless the additional control options do not improve the safety)."

Recommendation:

As stated above for content deviation 2, the manufacturer can justify ceasing further risk reduction where it is determined that the risk is acceptable, i.e. that risk reduction has progressed to a level as described above in the section of content deviation 3 .

The manufacturer shall consider all risk control measures in Essential Requirement 2 that are appropriate to reduce the risk to an acceptable level. In so doing, the manufacturer shall document the control options in the priority order, as part of the risk management process.

Compliance is checked by reviewing the documented risk management process.

<u>Content deviation 6:</u> Deviation as to the first risk control option

“inherent safety by design” vs. *“inherently safe design and construction”*

Recommendation:

The manufacturer shall ensure that, whenever possible, the first risk control option includes both safe design and safe construction.

Not relevant for compliance verification.

<u>Content deviation 7:</u> Information of the users influencing the residual risk

“..manufacturers shall not attribute additional risk reduction to the information given to the users...”

ISO 14971 (Annex J) and ISO/TR 24971 describe ‘information for safety’ as instructions for use, warnings, required maintenance, etc.. ‘Information for safety’ comprises instructions of what actions the user can take or avoid in order to prevent a hazardous situation from occurring. On the other hand, ‘disclosure of residual risk’ has the objective to inform users of remaining risk inherent to the use of the medical device, and concerns the risks remaining after all risk control measures have been taken.

Recommendation:

Any information for safety comprising instructions of what actions the user can take or avoid in order to prevent a hazardous situation from occurring may be considered a risk control measure. As required by Essential Requirement 13.1 of Directive 93/42/EEC (respectively ER B.8 of 98/79/EC) it may be considered as a risk control measure. The information includes the instructions for use, labels, etc.. Since ‘safe use’ is related to risk control measures, the Medical Device Directives do not deviate in that regard from EN ISO 14971. Any effects on risk reduction are to be documented by the manufacturer in the risk management file.

‘Disclosure of residual risk’ should be conducted in compliance with EN ISO 14971 Clause 6.4, 6.5 and 7. The manufacturer shall not claim a reduction to the probability of harm when disclosing residual risk.

Compliance is checked by inspection of the risk management file.

5.) Recommendations for the NB audit process

The role of the Notified Body is to assess compliance to the Directives, including the implementation of the risk management process and whether clinical benefits outweigh the risks to patients and users.

Manufacturers placing devices on the European market should be aware that gaps between the requirements of the Directives and the Risk Management Standard (documented in the EN ISO 14971: 2012 edition) have to be addressed, if applicable. It is the discretion of the manufacturer to use this standard in conjunction with other means to demonstrate conformity with the Essential Requirements of the Directive.

When EN ISO 14971 is used in upcoming audits and risk management file reviews, assessors and technical experts from Notified Bodies will focus on objective evidence on how manufacturers addressed those gaps and modified their Risk Management Process accordingly. More specifically they will evaluate:

1. Are all design solutions in conformity with the safety principles given in the Essential Requirements and EN ISO 14971 (inherent safe design and construction > protection measures > information for safety)?

2. Has the manufacturer demonstrated that all risks have been reduced to an acceptable level in the sense of this guidance paper?

3. Has the manufacturer conducted a risk benefit analysis for all individual residual risks that are not acceptable according to the risk acceptability criteria?
4. Has the manufacturer conducted an overall risk benefit analysis considering all individual risks combined?

5. Has the manufacturer demonstrated that information for safety is effective?

6. Has the manufacturer included information on residual risks, if needed, in the accompanying documents?

Annex 1: Recommendations for Standardization Bodies

Modification of IEC 60601-1 (Ed. 3.1)

Amendment A1:2012 to IEC 60601-1:2005 (together Edition 3.1) has improved the consistency of risk management terminology. Nevertheless, this edition has room for further improvement. The primary objective of the standard (and its collateral and particular standards) is to provide state-of-the-art requirements and solutions for basic safety and essential performance. The standard should be restrictive in referring to risk management.

Modification of EN ISO 14971

As has been argued, the Annexes Z to EN ISO 14971:2012 contain errors and occasionally confusing phrases. It is therefore important that these Annexes are amended through a revision of EN ISO 14971. This is within the remit of the European Standards Organizations and within CEN/CENELEC TC3 in particular. The joint Notified Bodies do not have an explicit role in this Technical Committee but, upon acceptance and implementation of this consensus paper, the NBRG is willing to contribute to amendment suggestions that subsequently may be taken forward by individual members of CEN/CENELEC TC3.

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