Impact of EN ISO 14971:2012 on Medical Device Risk Assessment in the EU

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ISO International Standard & EU Harmonization

International standard ISO 14971 - Medical devices - Application of risk management to medical devices was developed by the International Organization for Standardization (ISO) in 1998. It was written with participation from delegates representing 112 countries and has worldwide application to risk/benefit assessment. This standard is intended to provide manufacturers with a framework within which experience, insight, and judgment are applied systematically to manage the risks associated with the use of medical devices.

The ISO 14971 standard was last revised in 2007 and these requirements are still current. The European harmonized standard EN ISO 14971 was initially released in 2009 and recently revised in 2012. This latest 2012 revision has modifications that are intended to aid in the identification of remaining discrepancies between ISO 14971:2007 and the Essential Requirements for medical devices as contained in the preexisting EU directives (93/42/EEC on Medical Devices, 90/385/EEC on Active Implantable Medical Devices, and 98/79/EC on In Vitro Diagnostic Devices).

With the release of EN ISO 14971:2012, the requirements laid out in ISO 14971:2007 are still current because the normative text is the same between the two standards and these requirements provide the foundation for the subsequent regional or country-specific risk management standards. An EN document is developed as a “harmonized,” or accepted, regional standard applicable to the European Union (EU). EN documents are written under protocols with participation from delegates of the EU member states and must subsequently be adopted by each member state either with or without revisions. For example, DIN EN ISO 14971:2013 is the version adopted by Germany based on EN ISO 14971:2012 which is, in turn, based on ISO 14971:2007. Note that when a country chooses to adopt an ISO standard, they add a level of administrative overhead and thus the adopted versions typically have later issue dates than the original ISO document.

A harmonized EN ISO standard is accomplished via appendices (Informative Annex Z) that clarify any gaps or differences between the requirements of the worldwide ISO standard and those of the EEC medical device directives. In the case of EN ISO 14971:2012, while the normative text is the same as the ISO standard, the requirements are not because the EEC directives add a further level of compliance in key areas of risk assessment. The Annex Z requirements of the EN version are more stringent as compared to the ISO version; therefore, compliance with the ISO 14971 standard alone is not sufficient in the European arena. You must comply with the country-specific EN ISO 14971 standard for each country in which you plan to market your product.


So Which One Is the Real Standard?
The difficulties inherent in these sorts of harmonizations are apparent, and thus the EN ISO 14971:2012 standard states: “Because this is an international standard, intended to be applicable in jurisdictions all over the world, it is not the primary goal of the standard to cover exactly any of the European Essential Requirements.” In other words, in regards to the Essential Requirements, “conformity is not entirely achieved by complying only with the requirements specified in this standard.” Translation: companies marketing medical devices in the EU are responsible for adhering to EEC standards, not just ISO standards.

Table 1 identifies the aspects where the ISO standard deviates, or might be understood as deviating, from the European Essential Requirements thereby outlining the differing approaches to risk management.
### Table 1. Content Deviations between ISO 14971:2007 and Directive 93/42/EEC on Medical Devices

<table>
<thead>
<tr>
<th>ISO 14971:2007</th>
<th>EEC DIRECTIVE</th>
<th>INTERPRETATION</th>
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<tbody>
<tr>
<td><strong>NEGLIGENCE RISKS</strong></td>
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<td>Manufacturer may discard negligible risks [Annex D.8.2].</td>
<td>All risks, regardless of their dimension, need to be reduced as much as possible and need to be balanced, together with all other risks, against the benefit of the device [Annex I, Sections 1 and 2].</td>
<td>Manufacturer must take all risks into account.</td>
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<td><strong>ASSESSMENT OF RISK ACCEPTABILITY</strong></td>
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<td>Only non-acceptable risks are required to be integrated into the overall risk-benefit analysis [Annex D.6.1].</td>
<td>All risks, regardless of any “acceptability” assessment, must be reduced as far as possible and must be balanced, together with all other risks, against the benefit of the device [Annex I, Sections 1 and 2].</td>
<td>Risk acceptability may not be applied prior to applying Sections 1 and 2 of Annex I of Directive 93/42/EEC.</td>
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<td><strong>RISK REDUCTION</strong></td>
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<td>Risks must be reduced “as low as reasonably practicable” (ALARP) [Annex D.8]. The ALARP concept contains an element of economic consideration.</td>
<td>Risks are required to be reduced “as far as possible” without room for economic considerations [Annex I, Section 2].</td>
<td>Manufacturers and Notified Bodies MAY NOT apply the ALARP concept.</td>
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<td><strong>NEED FOR RISK-BENEFIT ANALYSIS</strong></td>
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<td>When specific residual risk (or overall residual risk) is judged not acceptable using risk management plan criteria and further risk control is not practicable, the manufacturer may determine if potential medical benefits outweigh the residual risk [Clauses 6.5 &amp; 7]. A risk/benefit analysis is not required by this International Standard for every risk [Annex D.6.1].</td>
<td>An overall risk-benefit analysis must take place, regardless of the application of criteria established in the management plan of the manufacturer [Annex I, Section 1]. Undesirable side-effects must “constitute an acceptable risk when weighed against the performance intended.” [Annex I, Section 6].</td>
<td>Individual and overall risk-benefit analyses are required in all cases.</td>
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<td><strong>RISK CONTROL OPTIONS/MEASURES</strong></td>
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<td>One or more risk control options are required, in this order: (a) inherent safety by design; (b) protective measures in the medical device itself or in the manufacturing process; (c) information for safety [Clause 6.2]. Further risk control measures do not need to be taken if, after applying one of these control options, the risk is judged acceptable according to the risk management plan [Clause 6.4].</td>
<td>“State of the art” in safety principles requires that all control options or control mechanisms be applied cumulatively [Annex I, Section 2].</td>
<td>The manufacturer must apply all control options even if previous control options have reduced the risk to an acceptable level.</td>
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<td><strong>SAFETY BY DESIGN</strong></td>
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<td>The first-priority measure, “inherent safety by design” [Clause 6.2], is not defined.</td>
<td>“Inherently safe design and construction” means that risks must be eliminated or reduced as far as possible [Annex I, Section 2].</td>
<td>Directive is more precise than Standard and thus Directive should be followed.</td>
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<td><strong>SAFETY INFORMATION &amp; RESIDUAL RISK REDUCTION</strong></td>
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<td>The third-priority measure, “information for safety” given to users, is regarded as a measure to reduce risk [Clause 6.4].</td>
<td>Users must always be informed about residual risks, and thus safety information given to users is not part of the risk reduction equation [Annex I, Section 2].</td>
<td>Manufacturers cannot use user training or Instruction for Use (IFUs) to accomplish reduction of residual risk.</td>
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**Summary of Deviations**

Although the Annex Z appendices to the EN ISO 14971:2012 standard bring ISO and EEC into closer agreement, the key discrepancies described above affect how risk/benefit is assessed and thus how medical devices are designed, manufactured, and marketed in the EU. In brief:

- All risks must be taken into account.
- A risk/benefit analysis must be conducted for all products and take into account all risks.
- All risks must be reduced as far as possible.
- All risk control options/measures must be taken.
- Risks need to be reduced by an inherently safe design and construction.
- Information to users is a requirement but does not reduce residual risk.

Again, Annex Z’s found in the EN standards must be taken into account when developing a device for the EU market. In the case of risk management, meeting the ISO 14971:2007 normative requirements alone is not enough to claim compliance to the EU Essential Requirements.

**Is Your Company in Compliance?**

So what does this mean regarding assessment and CE mark approval? Assessors will expect that manufacturers are aware of the gaps between the ISO requirements and those of the EEC Directives, that they have undertaken or are in the process of undertaking any actions needed to address the gaps, and that ultimately these gaps are addressed for all products with a CE mark. Notified Bodies will focus on compliance to the Directives and expect manufacturers to assess risk/benefit according to the Directives, not just according to ISO.

You may already be in compliance and your procedures and documents may be sufficient. However, a check of your internal procedures is advisable:

- Does your company have a procedure for dealing with new revisions of standards?
- Are you in compliance with your procedures?
- If possible have all risks been designed out?
- Have the risks been reduced as much as possible?
- Has a risk/benefit analysis been conducted that includes all risks?
- Have warnings and information provided in the IFUs and/or training processes been incorrectly assessed as reducing risk?

As these content deviations have been in effect for a relatively short period of time, they are still being discussed and their ramifications debated by medical device manufacturers and Notified Bodies. Since each Notified Body may interpret compliance to the content deviations differently, it would be a good idea to discuss the deviations with your Notified Body in advance of the next surveillance audit so that expectations are communicated and well understood.

**Resources**

