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## WHITEPAPER: Risk Management EN ISO 14971:2012 – Implications for Medical Device Manufacturers

White paper produced by Maetrics

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## Introduction

Risk management is a fundamental step for medical device manufacturers to demonstrate compliance with the EU Directives for medical devices, ensuring the safety of patients and users. Risk management has been conducted following the principles laid out in ISO 14971, yet since the advent of the new version of EN ISO 14971:2012 - *Medical devices – Application of risk management to medical devices*, the additional clarification within the standard has led to a number of misconceptions and confusion surrounding the implementation of the new standard by medical device manufacturers. Some frequently heard comments by manufacturers on the new versions of EN ISO 14971 are:

“We must use dFMEA (design failure mode and effect analysis) and pFMEA (production or process FMEA) from now on.”

“All identified risks must be eliminated.”

“We cannot use Annex C questions as we used to.”

“We can no longer use ALARP (as low as reasonably practicable) but must use ALAP (as low as possible).”

“All risks must be addressed by design changes from now on.”

“We will have to go back and rewrite all our risk files.”

“We are not allowed to put warnings in the IFU.”

As can be seen from the comments, medical device manufacturers have been left in some cases scratching their heads about how exactly they were going to implement the new standard. Did they need to rewrite all the risk analysis they had conducted so far or did they just have to apply the new version of the standard to future risk management activities? This white paper will help medical device manufactures understand the changes made to the EN harmonized version of ISO 14971:2012 and provide guidance on what is expected of medical device manufactures for compliance with the standard, thereby separating the facts from the misconceptions.

## Background

The current ISO (internationally recognized) version of the standard is ISO 14971:2007, which is recognized by the FDA for managing risks associated with medical devices. Any standard that carries the EN nomenclature indicates that it has been harmonized to one or all of the European Directives with respect to the Essential Requirements detailed within an annex of the specific EN standard.

The EN version of ISO 14971 had undergone a previous harmonization step in 2009 with the inclusion of three “Z” annexes that described the relationship between the standard and the three European Directives for medical devices. Essentially, compliance with the standard meant that all the Essential Requirements of the

directives relating to risk and/or safety were covered by complying with the EN ISO 14971 standard.

EN ISO 14971:2012 was published as a result of objections being raised by the Competent Authority in Sweden and the European Commission regarding the inconsistencies in the previous harmonized standard relating to the wording in the three “Z” annexes.

## New standard

The main contents of the new version of the standard have not changed. The additional wording has focused around the annexes listed at the front of the standard that explain the relationship of the standard to the relevant European Directives for medical devices. The risk management process has therefore remained the same, as reflected in the fact that the contents listed in the standard remain the same with the following clauses:

- Clause 1: Scope
- Clause 2: Terms and Definitions
- Clause 3: General Requirements, Including Planning
- Clause 4: Risk Analysis
- Clause 5: Risk Evaluation
- Clause 6: Risk Control
- Clause 7: Evaluation of Overall Residual Risk Acceptability
- Clause 8: Risk Management Report
- Clause 9: Production and Post-Production Information

Ten annexes provide informative guidance with the standard, including the risk assessment process, questions for identifying safety hazards, risk concepts, examples of hazards, a risk management plan, risk management techniques and specific guidance on in-vitro diagnostic devices, biological hazards and communicating residual risk safety information. In essence, the same steps are still taken by the manufacturer to conduct a risk assessment for a medical device, as follows:

- a) Create a risk management plan (Clause 3.4).
- b) Identify the device characteristics (Clause 4.2 and Annex C).
- c) Identify the hazard and estimate risks (Clauses 4.3 and 4.4).
- d) Evaluate the risks identified (Clause 5).
- e) Develop appropriate risk control measures (Clause 6).
- f) Evaluate the overall risk for those identified (Clause 7).
- g) Prepare a risk management report (Clause 8).
- h) Maintain the risk file by gathering data in the production and post-production phases (Clause 9).



## New Annexes

The main change has been the additional details incorporated into the Annexes ZA, ZB and ZC that demonstrate how the EN ISO 14971:2012 standard helps the manufacturer comply with the three European Directives for medical devices:

- Medical Devices Directive 93/42/EEC (by Annex ZA)
- Active Implantable Medical Device Directive 90/385/EEC (by Annex ZB)
- In Vitro Diagnostic Medical Device Directive 98/79/EC (by Annex ZC)

For ease of discussion, this white paper will refer to Annex ZA listed in the standard as the annex that relates to the Medical Devices Directive, and the same concept is used for the remaining directives detailed under Annexes ZB and ZC.

The table listed under the ZA Annexes of the standard helps to explain where the standard can be used and how far it goes in demonstrating compliance with the Essential Requirements detailed in the Medical Devices Directive. Where any discrepancies occur, they have also been highlighted. Unfortunately, the wording is based on an interpretation by an assessor reviewing both the standard and the directives. Hence, a literal interpretation has been taken, providing an extrapolated viewpoint instead of a practical approach of how to overcome the shortfalls, as evident in the discussion in table 1 of the “Z” Annexes as highlighted below.

Discussion in Table ZA 1 of ISO EN 14971:2012	Essential requirements wording (MDD)	Solution for Manufacturer
ER 1, ER 5 and ER 7.1 are not entirely covered by EN ISO 14971, since the standard does not cover requirements on design, manufacture, packaging and does not cover performances and characteristics related thereto.	The devices must be designed and manufactured in such a way that when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients.	The use of the questions listed in Annex C of the standard should be the starting point for manufacturers' risk analysis, which is to identify the characteristics of the device that may impact safety as expected by the standard and Notified Bodies.
Parts of ER 2 and ER 4 are not directly covered since the standard does not provide requirements on design	The solutions adopted by the manufacturer for the design and construction of the device must conform to	However, to address the shortfalls listed in Table 1 of the ZA Annex, the following should be

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<p>and constructions, nor does it apply the concept of 'safety principles' as intended in the MDD.</p>	<p>safety principles...</p> <p>The devices must be designed, manufactured and packed in such a way that their characteristics and performances...</p> <p>It appears that the commentary listed in the table has been used as the exact wording in the Essential Requirements yet has not been used in the standard. The intention of Essential requirement # 1, however, could be to indicate that devices are designed and are manufactured other than highlighting specific aspects of design and manufacture. The same principle is held for "safety principles" and packaging that are not included directly in the wording of the standard.</p>	<p>considered:</p> <ul style="list-style-type: none"> <li>a) As well as answering the Annex C questions, incorporate some questions around the design process and how failures in the design process could impact patient safety or produce other harm.</li> <li>b) For question C.2.28, which requires a new manufacturing process to be explained, this should be improved by adding questions about how manufacturing processes and failures could lead to patient or other harm.</li> <li>c) A question on packaging should be included as there is not a specific one listed in the Annex C questions.</li> <li>d) A separate study could be performed on design, manufacture and packaging instead of adding specific questions to those</li> </ul>

Discussion in Table ZA 1 of ISO EN 14971:2012	Essential requirements wording (MDD)	Solution for Manufacturer
		<p>listed in Annex C of the standard. This approach could be conducted using, for example, Failure Mode and Effect Analysis (FMEA).</p> <p>e) If FMEAs are performed, ensure that any residual risks found are transferred to the main risk table and are evaluated in the same manner as other risks.</p>

All of the clauses of the standard (1 – 9) are required to demonstrate compliance with the Essential Requirements of the European Directives. However, not all of the parts of the Essential Requirements are covered by the standard as highlighted in the table and additional documentation is required by the manufacturer to ensure full compliance with the essential requirements and hence the directives.

## Content Deviations

The content deviations expand on the requirements detailed in the table listed in the Z Annexes covering the three medical device directives, and they identify where the new standard's definitions or content deviate from the Essential Requirements. The shortfall of each content deviation will be explained and interpreted with a solution that the manufacturer can adopt to ensure compliance to the new standard is achieved.

Content Deviation Title	EN ISO 14971:2012 Clause interpretation	Interpretation of Essential Requirements	Solution for the Manufacturer
1 – Treatment of negligible risks	Clause D 8.2 The manufacturer may discard negligible risks.	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.	a) Instead of using “Insignificant” or “Acceptable” as the lowest category of risk defined within the plan, use the definition of “Low” as insignificant risk as detailed in D.8.5 of the standard. b) This “Low” risk category is not just to capture risks that are disregarded, and control measures should still try to be applied.
2 – Discretionary power of manufacturer as to the acceptability of risks	Clause 5, 6.1, 6.4, 6.5 and 7 Manufacturers have the freedom to decide upon the threshold for risk acceptability. Only non-acceptable risks have to be integrated into the overall risk-benefit analysis.	All risks have to be reduced as far as possible and that all risks combined, regardless of any “acceptability” assessment, need to be balanced, together with all other risks, against the benefit of the device.  There is a contradiction	c) The plan details that all risks will be investigated for further reduction and not just the ones falling in the “High” or “Low” category. d) The use of “Low”, “Medium” and

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		<p>between the standard and the Essential Requirements as all risks need to be reduced as far as possible, irrespective if they are negligible and fall below the threshold designated in the plan.</p>	<p>“High” risk categories is to try and prioritize the order for completing control measures and should be documented as such within the plan to indicate that all risks will be investigated for the potential of control measures.</p>
<p>3 – Risk reduction “as far as possible” versus “as low as reasonably practicable”</p>	<p>Clause 3.4 and D 8 contain the concept of reducing risks as low as reasonably practicable. The ALARP concept contains an element of economic consideration.</p>	<p>Eliminate or reduce risk as far as possible, without there being room for economic considerations</p> <p>The use of ALARP as a risk category to capture risks lying between “High” and “Low” risks is no longer advisable as the use of ALARP has a measure of economic consideration, which should not be used as a</p>	<p>a) Use the category of “Medium,” “Intermediate” or “Reduced as far as possible” to move away from the concept of ALARP to eliminate the possibility of an economic consideration being used as a reason not to introduce a control measure.</p> <p>b) Make sure that all potential control measures have been assessed for this “Medium” group of risks in the</p>



Content Deviation Title	EN ISO 14971:2012 Clause interpretation	Interpretation of Essential Requirements	Solution for the Manufacturer
		<p>reason not to introduce an effective control measure. For example, if a small risk reduction could be provided but only at a high level of cost via a re-design, then this could be seen as not being practicable and the control measure not adopted.</p>	<p>Risk Management file to negate the possibility of an assessor assuming that economic considerations have been used in the decision process.</p> <p>c) Have there been any solutions adopted on similar devices that could be used; if not, this helps to strengthen the decision that there is no suitable solution available to reduce the risk.</p> <p>d) By having detailed records of the decision process documented, this will help to support the decision that the risks were reduced "as far as possible." Any apparent decisions based on economic considerations can be easily assessed for compliance with the Essential Requirement by a third party during</p>

Content Deviation Title	EN ISO 14971:2012 Clause interpretation	Interpretation of Essential Requirements	Solution for the Manufacturer
			an audit.
4 – Discretion as to whether a risk-benefit analysis needs to take place	<p>Clause 6.5 and D 6.1</p> <p>An overall risk-benefit analysis does not need to take place if the overall residual risk is judged acceptable when using the criteria established in the risk management plan. A risk/benefit analysis is not required by this international standard for every risk.</p>	<p>An overall risk benefit analysis must take place in any case, regardless of the application of criteria established in the management plan of the manufacturer.</p> <p>It requires undesirable side effects to constitute an acceptable risk when weighed against the performance intended.</p> <p>In practice, a risk benefit analysis has not traditionally been carried out for all individual risks identified as detailed in the Essential Requirements; only the unacceptable</p>	<p>a) Always conduct a risk benefit analysis using accurate sources of data to draw conclusions on the clinical benefits.</p> <p>b) Traditionally, a spreadsheet has been used to record and score the risks; if this is the case, add an extra column after the residual risk has been calculated to provide commentary on the individual risks with respect to how the risk is outweighed by the benefit of the device.</p>

Content Deviation Title	EN ISO 14971:2012 Clause interpretation	Interpretation of Essential Requirements	Solution for the Manufacturer
		residual risks are assessed for risk benefit. This is not considered in compliance with the Essential Requirements.	
5 – Discretion as to the risk control options/measures	Clauses 6.2 and 6.4 oblige the manufacturer to use one or more of the following risk control options in the priority listed. They indicate that further risk control measures do not need to be taken if, after applying one of the options, this risk is judged acceptable according to the criteria of the risk management plan.	Must conform to safety principles, taking account of the generally acknowledged state of the art and to select the most appropriate solutions by applying cumulatively what has been called control options or control mechanisms.	<p>a) The three-level risk control hierarchy, which is described in the Risk Management plan, should also include information to state that the risk controls are applied cumulatively and so multiple control measures may be used for an individual risk.</p> <p>b) Ensure that in the risk table, where there are multiple control measures for a risk, they are described as such. For example, a design feature and alarm are used together to reduce the risk.</p>
6 – Deviation as to the first	Clause 6.2 obliges the	Eliminate or reduce risks as far	c) When reassessing the risk after control measures have

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risk control option	<p>manufacturer to use one or more of the following risk control options in the priority order listed: a) inherent safety by design, b) protective measures, c) information for safety, without determining what is meant by this term.</p>	<p>as possible (inherent safe design and construction).</p> <p>There is a conflict between the wording of the standard and the Essential Requirements; namely, the difference is between the implication of “inherent safety by design” and “eliminate and reduce risks as far as possible” (inherent safe design and construction). In addition, the control measures listed under content deviation point 5 are to be used by priority “in the following order” and are implied to be used cumulatively rather than individually.</p>	<p>been applied, ensure that the cumulative effect for numerous control measures has been considered in the scoring of the risk.</p> <p>d) Always refer to the Essential Requirements rather than the standard for clarification. For example, ensure that the first control measure used takes into account the wording of Essential Requirements #2: “safety by design and construction.”</p>

Content Deviation Title	EN ISO 14971:2012 Clause interpretation	Interpretation of Essential Requirements	Solution for the Manufacturer
7 – Information of the users influencing the residual risk	Clause 2.15, 6.2 and 6.4 Residual risk is defined as the risk remaining after application of risk control measures. This regards information on safety as a control option.	<p>Users shall be informed about the residual risks, indicating that the information given the user does not reduce the residual risk any further.</p> <p>The view point of this content deviation is that a warning in either the IFU or on the device or other literature supplied to the patient or user is not considered a risk reduction as the Essential Requirements state that the user must be informed of any residual risk.</p>	<p>a) A statement in the Risk Management Plan should be included to indicate that warnings alone will not be used as a control measure, but can be used to inform the user of any residual risk remaining for the device.</p> <p>b) Where a warning has been used, the risk reduction recorded in the table can only be from other classes of control options as described above and not from the application of the warning.</p> <p>c) In cases where a warning is applied directly to the device, such as “Do not touch – This part is hot,” then any risk reduction claimed must be verified using appropriate usability or user studies to generate</p>

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			<p>accurate data on risk reduction.</p> <p>d) If user training is required to ensure that any risks are conveyed to the user during the intended use of the device, then a suitable method of determining the effectiveness of the training is required to demonstrate an accurate value for scoring any risk reduction.</p>

## Discussion

Applying EN ISO 14971:2012 for new devices should be straightforward by implementing and following the newest revision of the standard as they conduct their risk management activities. However, the existing manufacturer's risk management files will have been approved by the Notified Body during conformity assessment procedures and surveillance audits with a risk management file that complied with an older version of ISO 14971. So with the advent of EN ISO 14971:2012, what are the implications for the manufacturer's existing risk management files with respect to Competent Authority and Notified Body expectations?

If the manufacturer has not taken account of the new annexes of ZA, ZB or ZC into the existing risk management files, then the manufacture will not be in compliance with the essential requirements of the directives. In addition, production and post-production controls (clause 9 of EN ISO 14971:2012) points to the fact that new or revised standards should be considered when updating or may trigger an update to the risk management file.

One of the easiest ways to conduct this task and demonstrate to the Competent Authority or Notified Body that the new standard has been reviewed is to conduct a gap analysis of the risk management files to the new standard. The gap analysis will identify areas for correction that can be incorporated into a plan.



## Conclusion

As this white paper has discussed, some realistic measures can be taken to overcome the weaknesses in the standard described in the “Z” annexes of EN ISO 14971:2012. The main points that may help medical device manufacturers with implementing the standard are:

1. Risk analysis for design, production and packaging using a suitable risk analysis tool is required to meet the directive requirements and must be considered in any risk evaluations.
2. All risks need to be reviewed and therefore no risks are discarded no matter how small the risk is evaluated to be.
3. Economic considerations must not be an input into the implementation of control measures if the control measure would be effective at reducing the risk.
4. Risks must be assessed against the benefits of using the device.
5. Risk/benefit analysis should always be conducted for the overall residual risk.
6. The three categories of control measure should always be investigated:
  - a. Inherent safety by design.
  - b. Protective measures in the medical device itself or in the manufacturing process.
  - c. Information for safety.
7. Any risk control measures or warnings incorporated into the IFU or other information supplied to the user cannot be considered to reduce the risk unless it can be proven.
8. Always refer back to the Essential Requirements of the directives for clarity instead of just relying on the standard.



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