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

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Introduction

Risk Management is a fundamental step for Medical Device Manufactures to demonstrate compliance to 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, 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 Manufactures. 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 it can be seen from the comments Medical Device Manufacturers were left in some cases scratching their heads about how exactly they were going to implement the new standard, did they need to re-write 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 to understand the changes made to the EN harmonised version of ISO 14971:2012, and provide guidance on what is expected of the Medical Device Manufacture to comply with the standard, thereby determining the facts from the myth.

Background

The current ISO (Internationally recognised) version of the standard is ISO 14971:2007, which is recognised by the FDA for managing risk associated with Medical Devices. Any standard that carries the EN nomenclature indicates that it has been harmonised 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 harmonisation 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 harmonised 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 been 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 which is reflected in the fact that the contents listed in the standard remains 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

There are ten annexes that provide informative guidance with the standard, including risk assessment process, questions to identify safety hazards, risk concepts, examples of hazards, 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 around additional detail incorporated into the Annexes, ZA, ZB and ZC that demonstrate how the EN ISO 14971:2012 standard helps the manufacturer to comply with the three European Directives for Medical Devices.


For ease of discussion this White Paper will refer to Annex ZA listed in the standard which relates to the Medical Devices Directive, for 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 to the Essential Requirement detailed in the Medical Devices Directive. Where there are any discrepancies this has also been highlighted, unfortunately the wording is based on an interpretation by an assessor reviewing both the standard and the directives and hence a literal interpretation has been taken, an extrapolated viewpoint instead of a practical approach of how to overcome the shortfalls, this is evident in the discussion in table 1 of the “Z” annexes as highlighted below.

<table>
<thead>
<tr>
<th>Discussion in Table ZA 1 of ISO EN 14971:2012</th>
<th>Essential requirements wording (MDD)</th>
<th>Solution for Manufacturer</th>
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<tr>
<td>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.</td>
<td>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...</td>
<td>The use of the questions listed in annex C of the standard should be the starting point for Manufacturers for their risk analysis, to identify the characteristics of the device that may impact on safety as expected by the standard and Notified Bodies. However, to</td>
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<td>are not directly covered since the standard does not provide requirements on design and constructions, nor does it apply the concept of ‘safety principles’ as intended in the MDD.</td>
<td>by the manufacturer for the design and construction of the device must conform to safety principles... The devices must be designed, manufactured and packed in such a way that their characteristics and performances... It appears that the commentary listed in the table has been used as the exact wording in the Essential Requirements 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</td>
<td>address the short falls listed in table 1 of the ZA annex, the following should be considered: 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 harms. b) For question C.2.28 which requires 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 harms. c) A question on packaging should be included as there is not a specific one listed in the Annex C questions.</td>
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All of the clauses of the standard (1 – 9) are required to demonstrate compliance to 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 to 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 identifies where the standard deviates in definitions or content from the Essential Requirements. The shortfall for
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.

<table>
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<tr>
<th>Content Deviation Title</th>
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<tr>
<td>1 – Treatment of negligible risks</td>
<td>Clause D 8.2 The manufacturer may discard negligible risks.</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</td>
<td>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.</td>
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<td>2 – Discretionary power of manufacturer as to the acceptability of risks</td>
<td>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.</td>
<td>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</td>
<td>b) This “Low” risk category is not just to capture risks that are disregarded but control measures should still try to be applied. c) The plan details that all risks will be investigated for further reduction and not just the ones falling in the “High” or “” category. d) The use of “Low”, “Medium” and</td>
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<td>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.</td>
<td>“High” risk categories is to try and prioritise 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.</td>
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<tr>
<td>3 – Risk reduction “as far as possible” versus “as low as reasonably practicable”</td>
<td>Clause 3.4 and D 8 Contains the concept of reducing risks as low as reasonably practicable. The ALARP concept contains an element of economic consideration.</td>
<td>Eliminate or reduce risk as far as possible, without there being room for economic considerations. 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</td>
<td>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. b) Make sure that all potential control</td>
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<td>a measure of economic consideration which should not be used as a 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</td>
<td>measures have been assessed for this “Medium” group of risks in the Risk Management file to negate the possibility of an assessor assuming that economic considerations have been used in the decision process.</td>
<td>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.</td>
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<td>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</td>
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<td>apparent decisions based on economic considerations can be easily assessed for compliance with the Essential Requirement by a third party during an audit.</td>
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4 – Discretion as to whether a risk-benefit analysis needs to take place

- Clause 6.5 and D 6.1
- 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...

- 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. Requires undesirable side effects to constitute an acceptable risk when weighed against the performance intended...

- a) Always conduct a risk benefit analysis using accurate sources of data to draw conclusions on the clinical benefits.
- b) Traditionally a spreadsheet has been used to record the 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...
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<td>every risk.</td>
<td>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 residual risks are assessed for risk benefit, this is not considered in compliance with the Essential Requirements.</td>
<td>risk is outweighed by the benefit of the device.</td>
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<td>5 – Discretion as to the risk control options/measures</td>
<td>Clauses 6.2 and 6.4 Obliges the manufacturer to use one or more of the following risk control options in the priority listed. Indicates that further risk</td>
<td>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</td>
<td>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</td>
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<td>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.</td>
<td>has been called control options or control mechanisms</td>
<td>measures may be used for an individual risk.</td>
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<tr>
<td>6 – Deviation as to the first risk control option</td>
<td>Clauses 6.2 Obliges the 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</td>
<td>Eliminate or reduce risks as far as possible (inherent safe design and construction) There is a conflict between the wording of the standard and the Essential Requirements, namely the difference is between the implication of</td>
<td>b) Ensure that in the risk table, that where there are multiple control measures for a risk that they are described as such for example a design feature and alarm are used together to reduce the risk. c) When re-assessing the risk after control measures have been applied, ensure that the cumulative effect for numerous control measures has been considered in the re-scoring of the risk. d) Always refer to the Essential Requirements rather than the standard for</td>
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| by this term.           | “inherent safety be 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. | 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>| 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. Regards Users shall be informed about the residual risks, indicating that the information given to the user does not reduce the residual risk any further | 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... |</p>
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<td>information for safety to be a control option.</td>
<td>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</td>
<td>any residual risk remaining for the device.</td>
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<tr>
<td>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.</td>
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<tr>
<td>c) In cases where a warning is applied directly to the device for example “Do not touch – This part is hot”, then any risk reduction claimed must be verified using appropriate usability or user studies to generate accurate data on risk reduction.</td>
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<td>d) If user training is required to ensure that any risks are conveyed to the</td>
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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, as 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 manufacturer 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 which can be incorporated into a plan.

**Conclusion**

As this white paper has discussed there are some realistic measures that 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 Manufacturer’s with implementing the standard are:

1. Risk analysis for design, production and packaging using a suitable risk analysis tool are required to meet the directive requirements and must be considered in any risk evaluations.
2. All risk 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 in 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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