8th Annual FDA Inspections Summit

Assuring Your EN ISO 14971:2012 Risk Management Strategy Adopts a holistic Approach

Ibim Tariah Ph.D
BSI Group Americas Inc

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Risk Management - Impact of Annex Z's

- Overview of ISO 14971:2007
- EN ISO 14971:2012
  - Harmonized Standard – Differences from ISO Standard
  - Deviations – Presumption of Conformity
- Notified Body Audit Questions
- Notified Body Holistic Approach

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ISO 14971:2007

Definitions

Risk = Combination of the **probability of occurrence of harm** and the **severity of that harm**

Harm = Physical injury or damage to the health of people, or damage to property, or the environment

ISO 14971 – Main body (Clauses 1-3)

1 Scope

2 Terms and definitions

3 General requirements for risk management

- 3.1 Risk management process
- 3.2 Management responsibilities
- 3.3 Qualification of personnel
- 3.4 Risk management plan
- 3.5 Risk management file

4. Annexes: A to J

ISO 14971 – Main body (Clauses 4-9)

Clause 4: Risk analysis

Clause 5: Risk evaluation

Clause 6: Risk control

Clause 7: Residual risk evaluation

Clause 8: Risk management report

Clause 9: Post-production information

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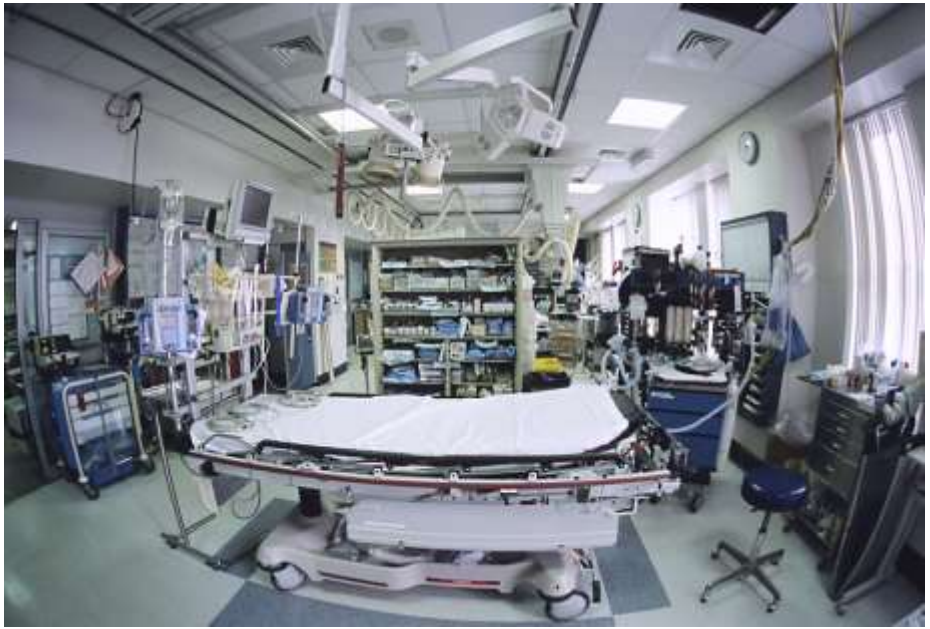
Risk Management – EU Requirements

Medical Devices – EU Risk Requirements

Risks > Benefits



Benefits > Risks

The Directives – Where is 'Risk'?

	MDD 93/42/EEC	AIMDD 90/385/EEC	IVDD 98/79/EC
"Risk"	ERs: 1 2 6 7.2, 7.4, 7.5, 7.6 8.1, 8.6 9.2, 9.3 11.2, 11.4 12.1, 12.5, 12.6, 12.7 13.5, 13.6	ERs: 1 5 8 9 10 11 15	ERs: A – 1 2 B – 1.2 2.1, 2.2, 2.5, 2.7 3.2, 3.3, 3.4 5.3 6.2, 6.3, 6.4 7.1 8.6, 8.7
Total	**41**	**18**	**24**

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EN ISO 14971:2012

- EU harmonized standard for Risk Management
- Allows the presumption of conformity to MDD, AIMDD, and IVD
- Published July 2012 & ha… 012.

ESO (1)	Refere…		of cessation of presumption of conformity of superseded standard Note 1
CEN	…ent to medical …version 2007-10-01)	30.8.2012	EN ISO 14971:2009 Note 2.1	Date expired (30.8.2012)

EN ISO 14971:2012 only applies to manufacturers placing medical devices on the market in Europe

http://ec.europa.eu/enterprise/policies/european-standards/harmonised-standards/medical-devices/index_en.htm

What is the difference?

ISO 14971:2007

- The current International Standard

EN ISO 14971:2009

- The previous version of the European Harmonized Standard
- Obsolete as of 30 August 2012

EN ISO 14971:2012

- The current European Harmonized Standard
- Changes within Foreword & Annex Zs only
- **No change** to requirements (Normative Text)
- i.e. clauses or requirements of the standard are exactly the same

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Why was EN ISO 14971:2012 created?

- A solution to formal objections raised by Swedish Competent Authority & European Commission on the harmonized status of a number of European Standards

- Revision of Annex Z's was made to provide greater clarity on applicability & alignment of ISO 14971 clauses with requirements of AIMDD, MDD & IVDD

EN ISO 14971:2012 – Z Annexes

Example – Annex ZA (MDD)

- "Explains to which requirements, under which conditions and to what extent **presumption of conformity** can be claimed."

Table ZA.1 — Correspondence between this European Standard and Directive 93/42/EEC

Clause(s)/subclause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
1-9	1	ER 1 is not directly covered by EN ISO 14971, since the standard does not provide requirements on design and manufacture. However, the standard provides a tool to generate the information that is a necessary preliminary step for a manufacturer to demonstrate that the device is in conformity with ER 1. For content deviations, see points 1, 2, 3, 4 below.

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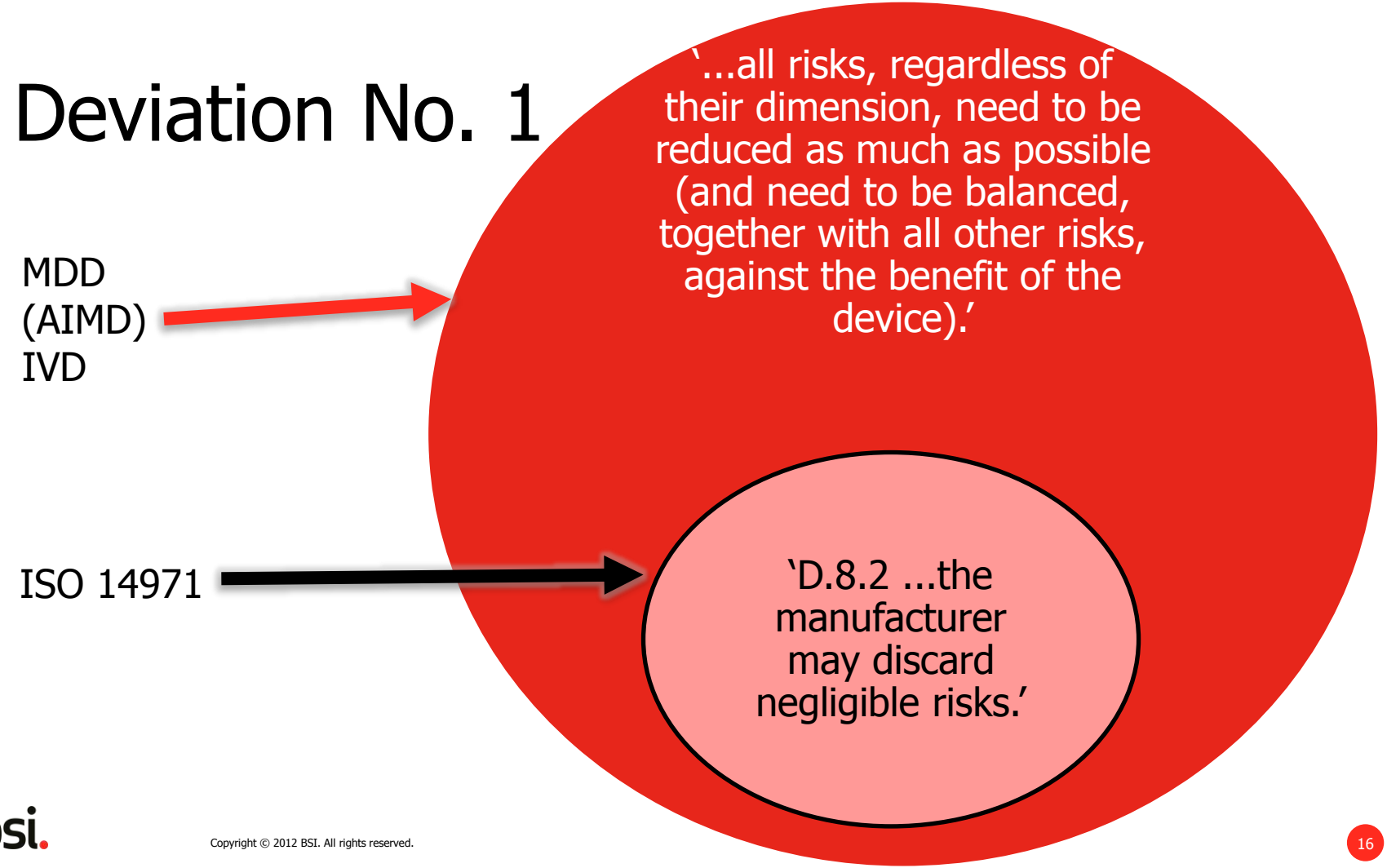
EN ISO 14971:2012 – Content Deviations

EN ISO 14971:2012 – Content Deviations

	Essential Requirements (ERs) Impacted		
Deviation	**MDD**	**AIMDD**	**IVDD**
1 – Treatment of negligible risks	1, 2, 6, 7.1	1, 5, 9	A.1, A.2, B.1.1
2 – Discretionary power of mfr as to acceptability of risks	1, 2, 6, 7.1	1, 5, 9	A.1, A.2, B.1.1
3 – Risk reduction "as far as possible" vs "as low as reasonably practicable"	1, 2, 6, 7.1	1, 5, 6, 9	A.1, A.2, B.1.1
4 – Discretion as to whether a risk-benefit analysis needs to take place	1, 6, 7.1	5 & 9	A.1 & B.1.1
5 – Discretion as to the risk control options / measures	2 & 7.1	-	A.2 & B.1.1
6 – Deviation as to the first risk control option	2 & 7.1	-	A.2 & B.1.1
7 – Information of the users influencing the residual risk	2 & 7.1	-	A.2 & B.1.1

Deviation No. 1



Were risks reduced as far as possible?

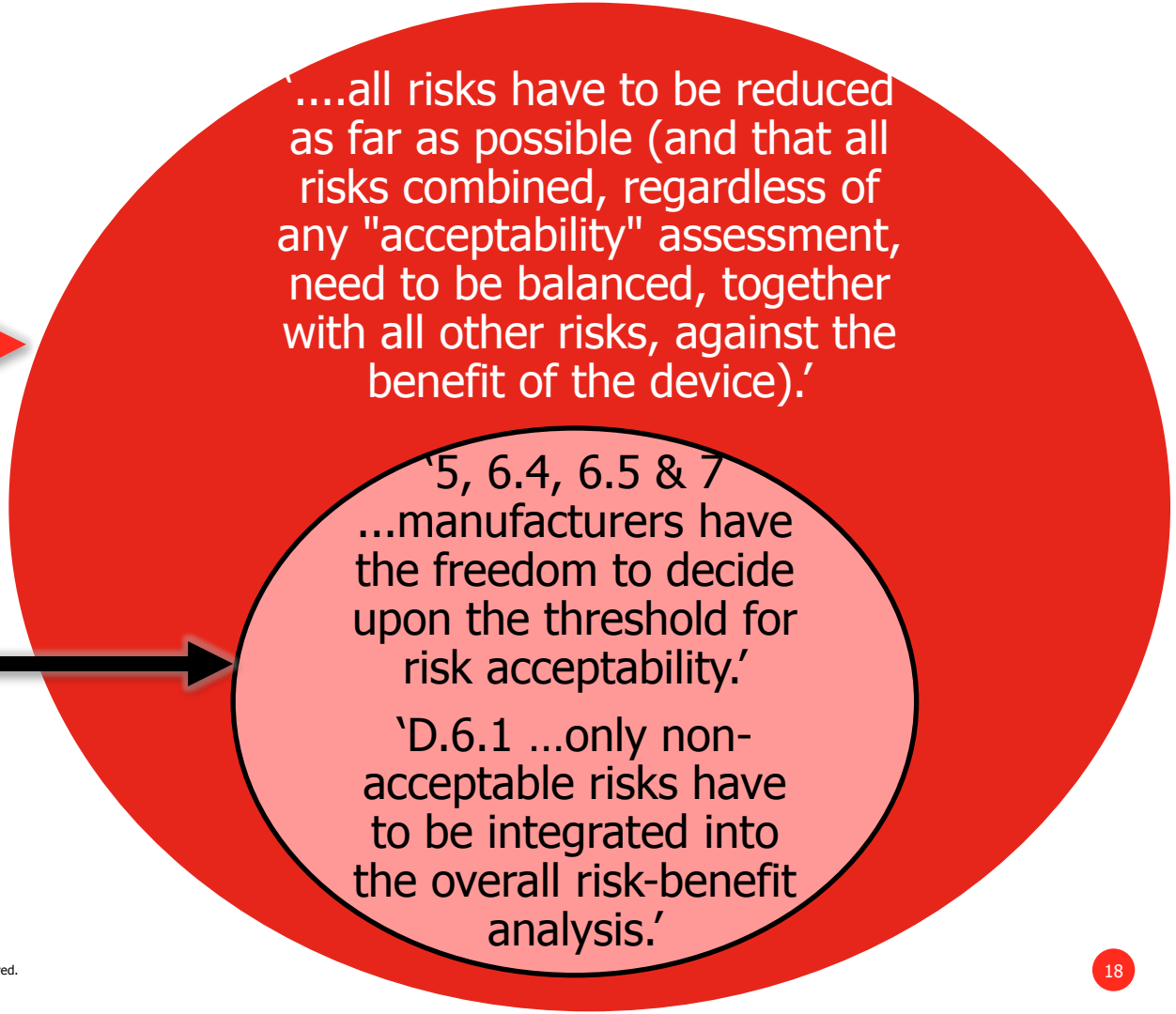
	Failure Mode	Cause of Failure	Local Effect	System Effect	Initial Rating			Risk Control Measure(s)	Risk Level
					SEV	PRO	RPN		
Hip Stem	Surgeon implants a stem that is wrongly sized	No tool available to determine needed size	Unstable Implant	Revision	8	1	8	X-ray templates provided for each implant size; implants marked with size; clinical history of safety / performance	Broadly Acceptable

It is not sufficient just to determine that the risks are acceptable. It is also necessary to determine whether they have been reduced as far as possible. This can be stated line-by-line or categorically as a whole.

Deviation No. 2

MDD
(AIMD)
IVD

ISO 14971



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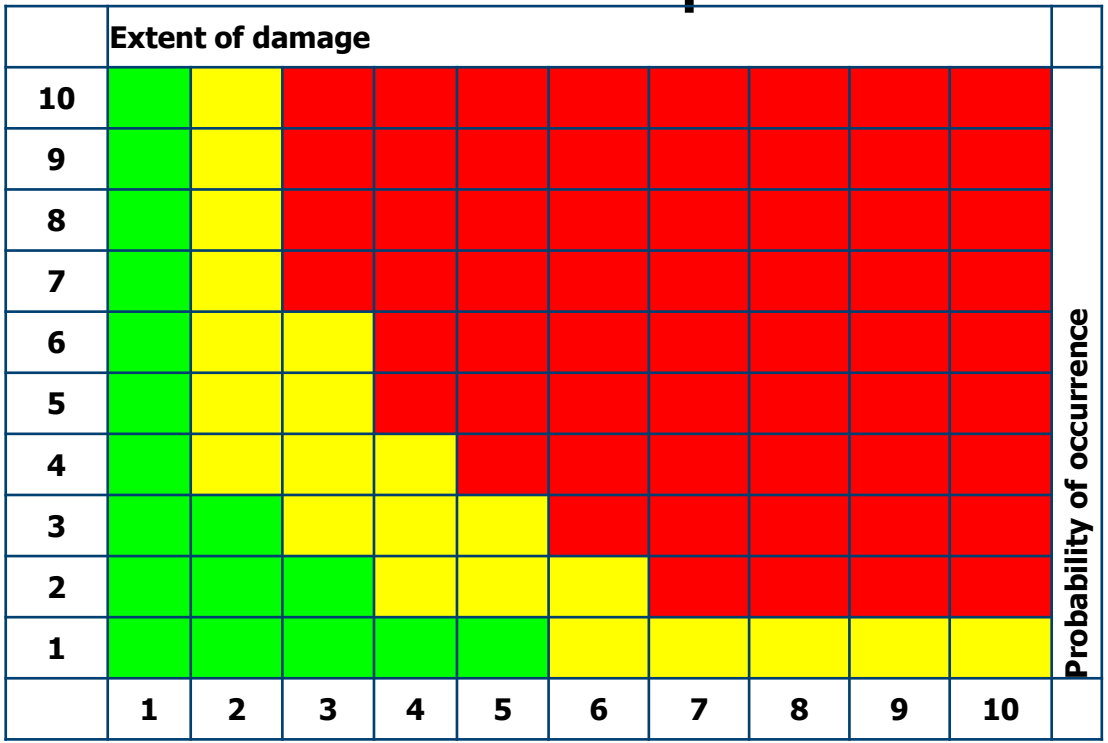
Are all risks reduced as far as possible?

Unacceptable

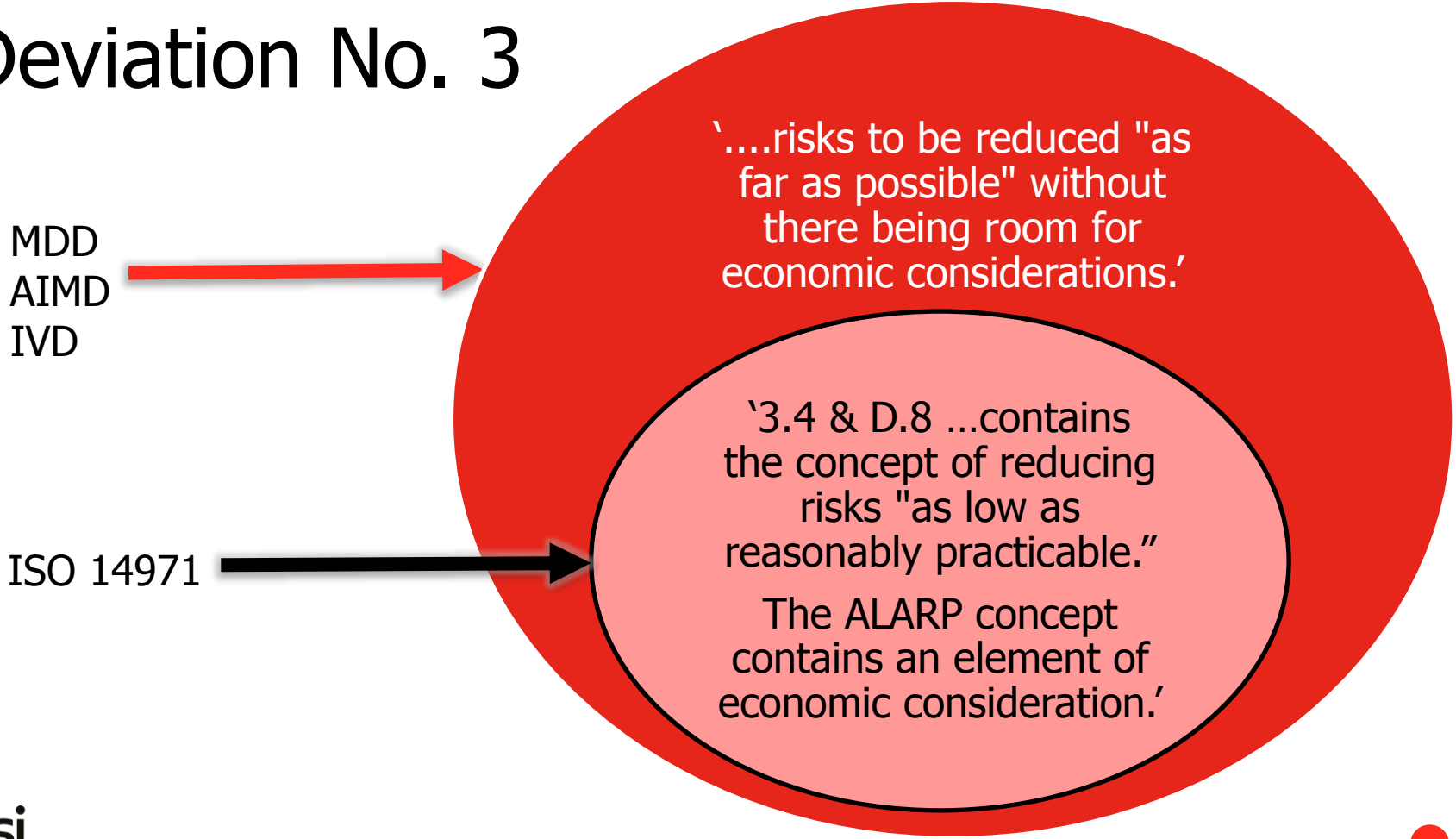
Management Review Required - ALARP

Broadly Acceptable

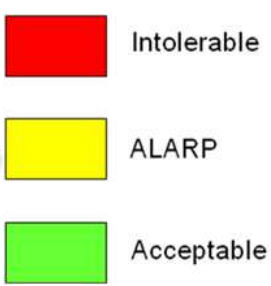
Some risks cannot be categorically ignored if risk can be reduced further. All risks must be reduced as far as possible.



Deviation No. 3



Are all risks reduced as far as possible?



There must another step – ALARP concept cannot be applied in isolation, risks must be reduced as far as possible

Probability of occurrence	Extent of damage									
10										
9										
8										
7										
6										
5										
4										
3										
2										
1										
	1	2	3	4	5	6	7	8	9	10

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Were risks reduced as far as possible?

	Failure Mode	Cause of Failure	Local Effect	System Effect	Initial Rating			Risk Control Measure(s)	Risk Level
					SEV	PRO	RPN		
Hip Stem	Surgeon implants a stem that is wrongly sized	No tool available to determine needed size	Unstable Implant	Revision	8	5	40	X-ray templates provided for every-other implant size; implants marked with size	ALARP

It is not reasonable in this example not to provide templates for each size. The economic impact of this should not be considered if this can reduce the risk. To make this determination, the state-of-the-art and available technology should be considered.

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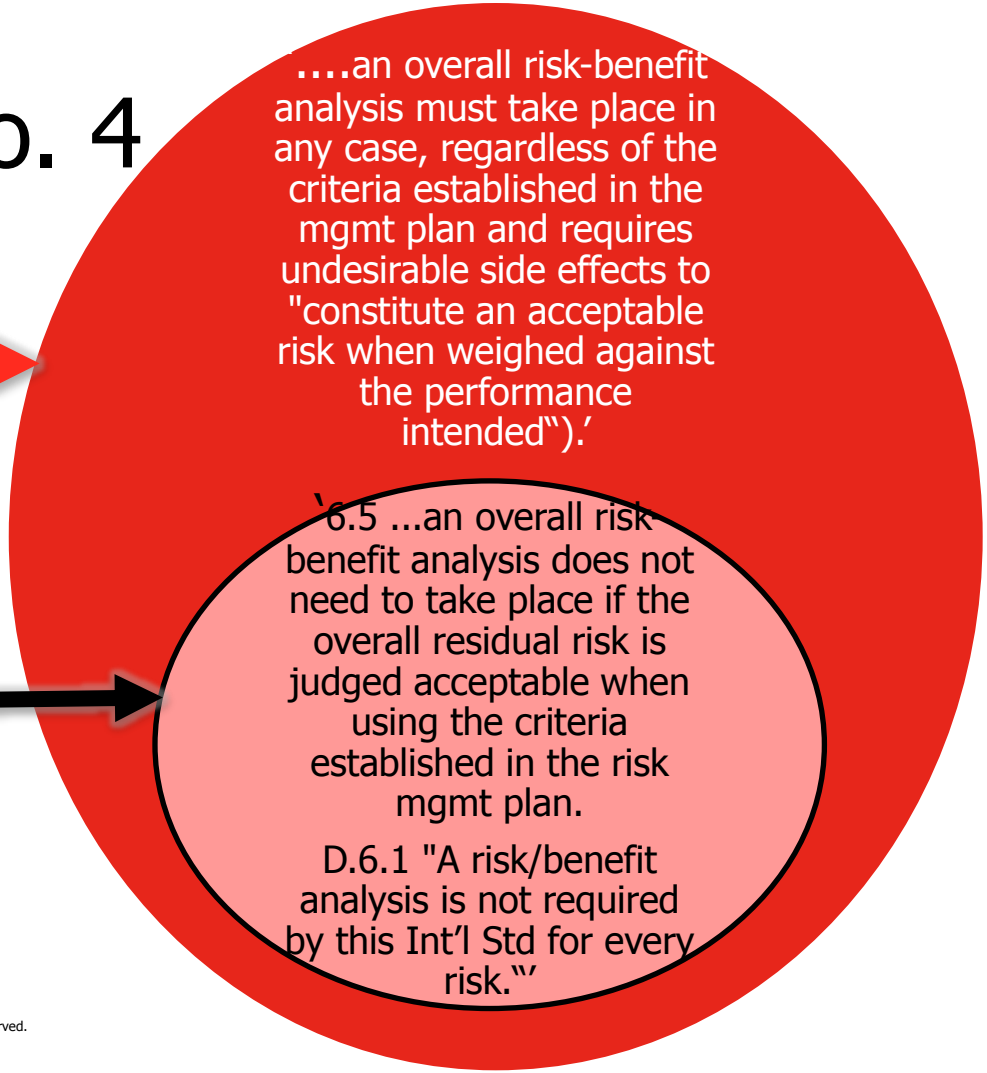
Deviation No. 4

MDD
AIMD
(IVD)

ISO 14971



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The Directives – Where is 'Benefit'?

	MDD 93/42/EEC	AIMDD 90/385/EEC	IVDD 98/79/EC
"Benefit"	ERs: 1 7.4 11.2	ERs: 10	ERs: A – 1
Total	**3**	**1**	**1**
"Risk"	**41**	**18**	**24**

MEDDEV 2.7.1 – Guidelines on Clinical Evaluation Report also discusses Risk / Benefit Analysis

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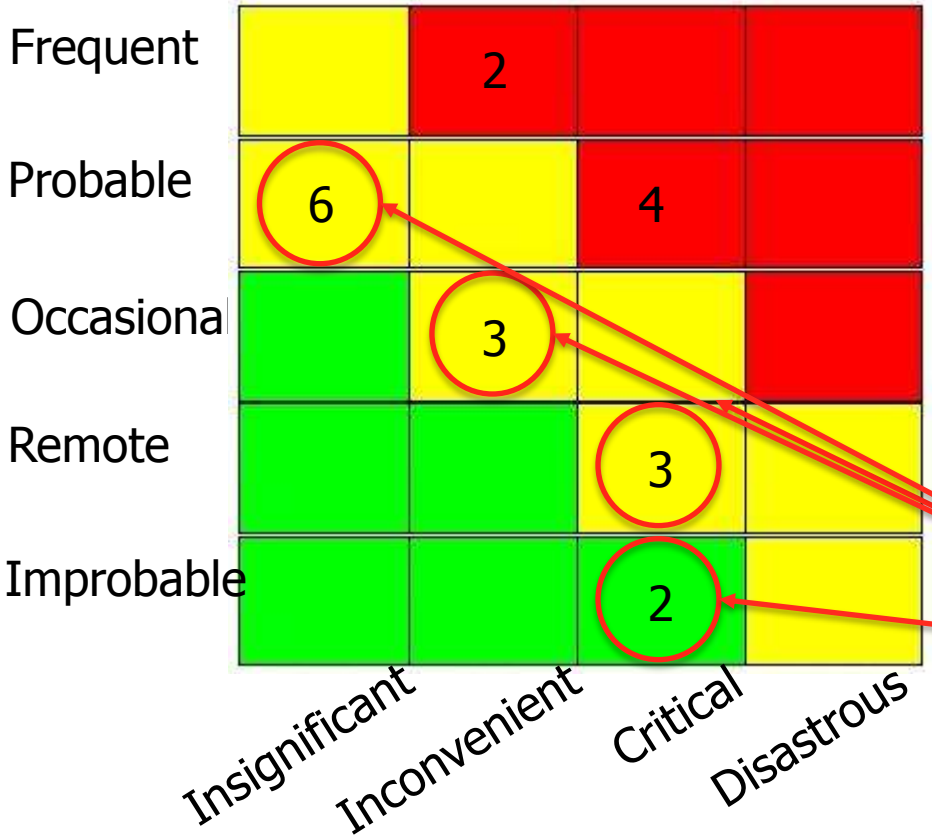
Risk / benefit analysis done for all risks?



Conduct Risk v Benefit

Consider Risk v Benefit

Acceptable

There must be a risk benefit analysis for all risks and an overall risk benefit analysis

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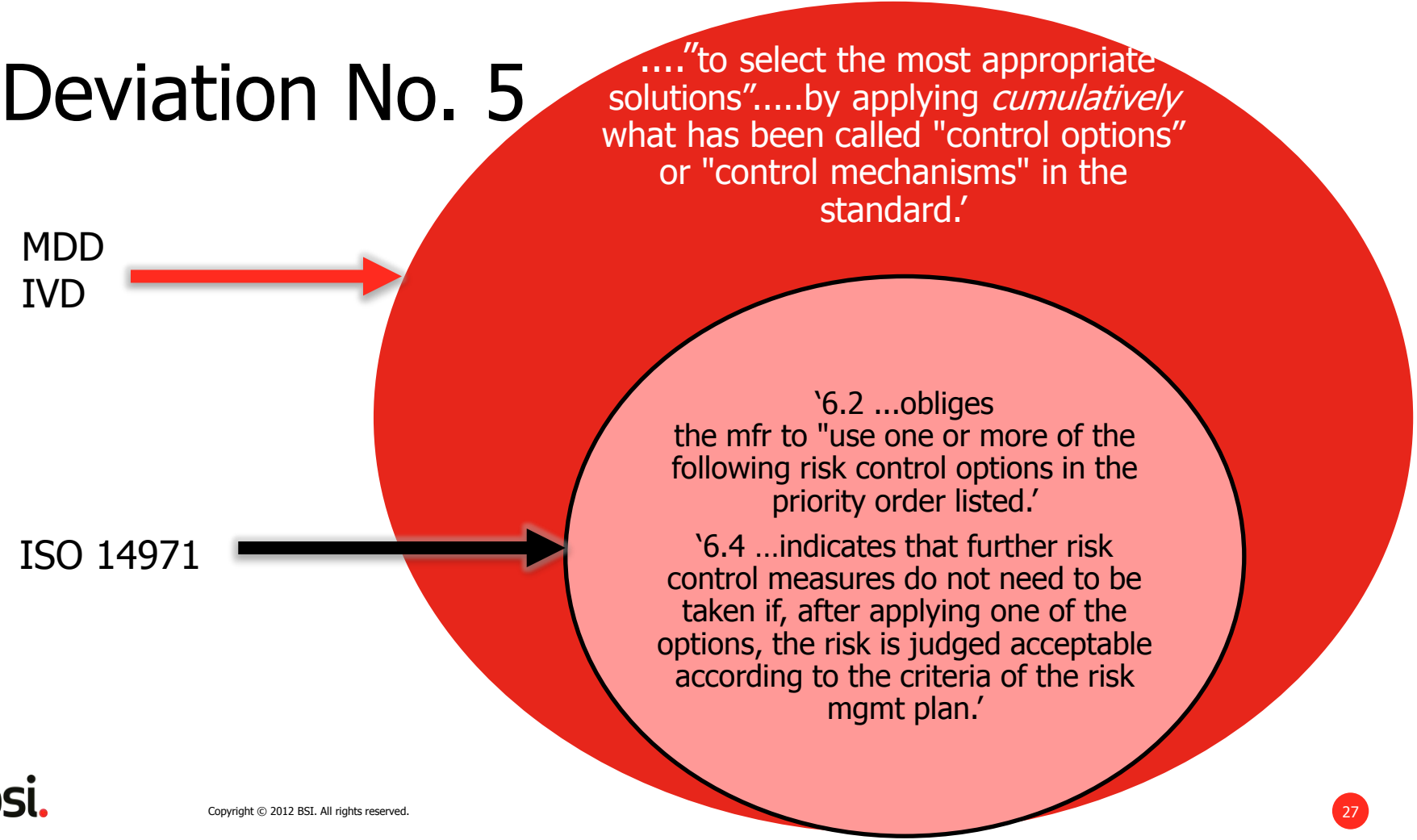
Documentation of Risk / Benefit Analysis

- Risk Management File
  - Combination of risk assessment / risk management report
- Clinical Evaluation Report (Frequently addressed here)

Deviation No. 5

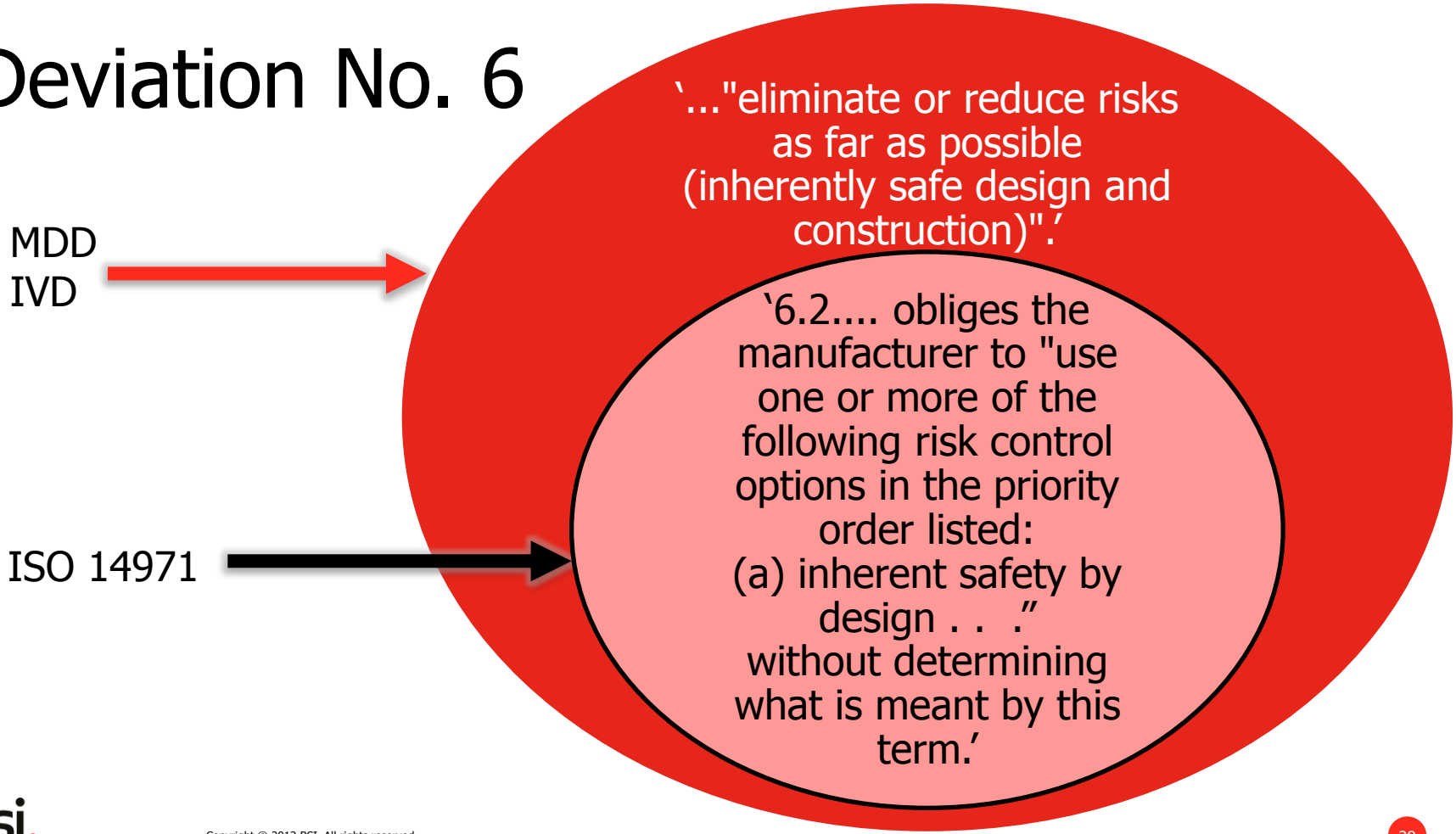


All appropriate controls utilized?

	Failure Mode	Cause of Failure	Local Effect	System Effect	Initial Rating			Risk Control Measure(s)	Risk Level
					SEV	PRO	RPN		
Intra-cranial Pressure Monitor	High pressure undetected	Monitor does not indicate high pressure situation	Brain damage	Death	10	4	40	Monitor provides continuous digital display of ICP; operates on AC & for up to 3 hrs on battery	ALARP

No control measures mentioned about alarms / warnings for high pressure situation. The current mitigation is not considered to be sufficient as preventive measures could mitigate the risk.

Deviation No. 6

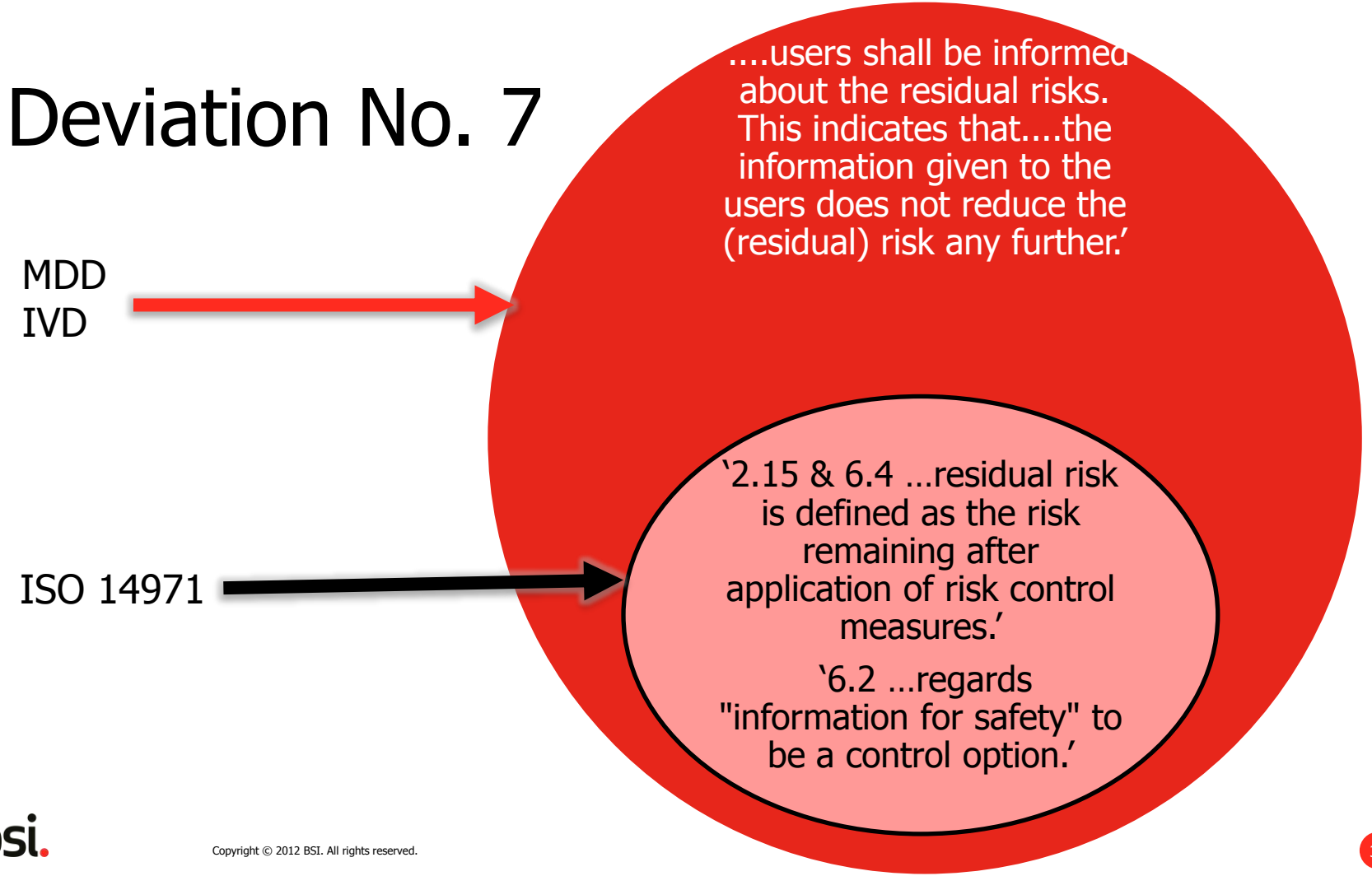


Were risks designed out if possible?

	Failure Mode	Cause of Failure	Local Effect	System Effect	Initial Rating			Risk Control Measure(s)	Risk Level
					SEV	PRO	RPN		
Mesh	Mesh frays and suture pulls out	Design of mesh / cutting edge	Failed repair	Revision	7	5	35	IFU instructs not to cut mesh and not to place sutures closer than 5 mm to edge	Acceptable & reduced as far as possible

Risks must be designed out if possible. All risk control options must be applied until risks have been reduced as much as possible and any additional control option(s) do not improve the safety

Deviation No. 7



Residual risks incorrectly reduced?

Device	Failure Mode	Effect	Initial Rating			Risk Control	Updated Rating		
			SEV	PRO	RPN		SEV	PRO	RPN
Implant	Emboli	Death	4	3	12	IFU warning	4	1	4

A warning does not reduce the probability of occurrence of an emboli.

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Notified Body Audit Questions

Notified Body Audit – Key Questions

- Are you aware of EN ISO 14971:2012?
  - How are you ensuring you meet the directive requirements?
- Have you reviewed your existing Risk Management files, if needed?
  - Is there a plan in place to do so?

BSI Audit – Key Questions

- Have all risks been reduced as far as possible?
- Has a risk benefit analysis been conducted for all risks?
- Have all risks been designed out if possible?
- Have risks been incorrectly reduced by warnings placed on IFUs or provided in training?

Notified Body Audit – Holistic Approach

- *ER 6 – Risk: Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended.*
- *ER 6a. Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X*.
  - Risk Management, including……
  - Post Market Surveillance and…..
  - Clinical Evaluation

Questions

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