

# 8<sup>th</sup> 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

# 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



...making excellence a habit.™

# 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

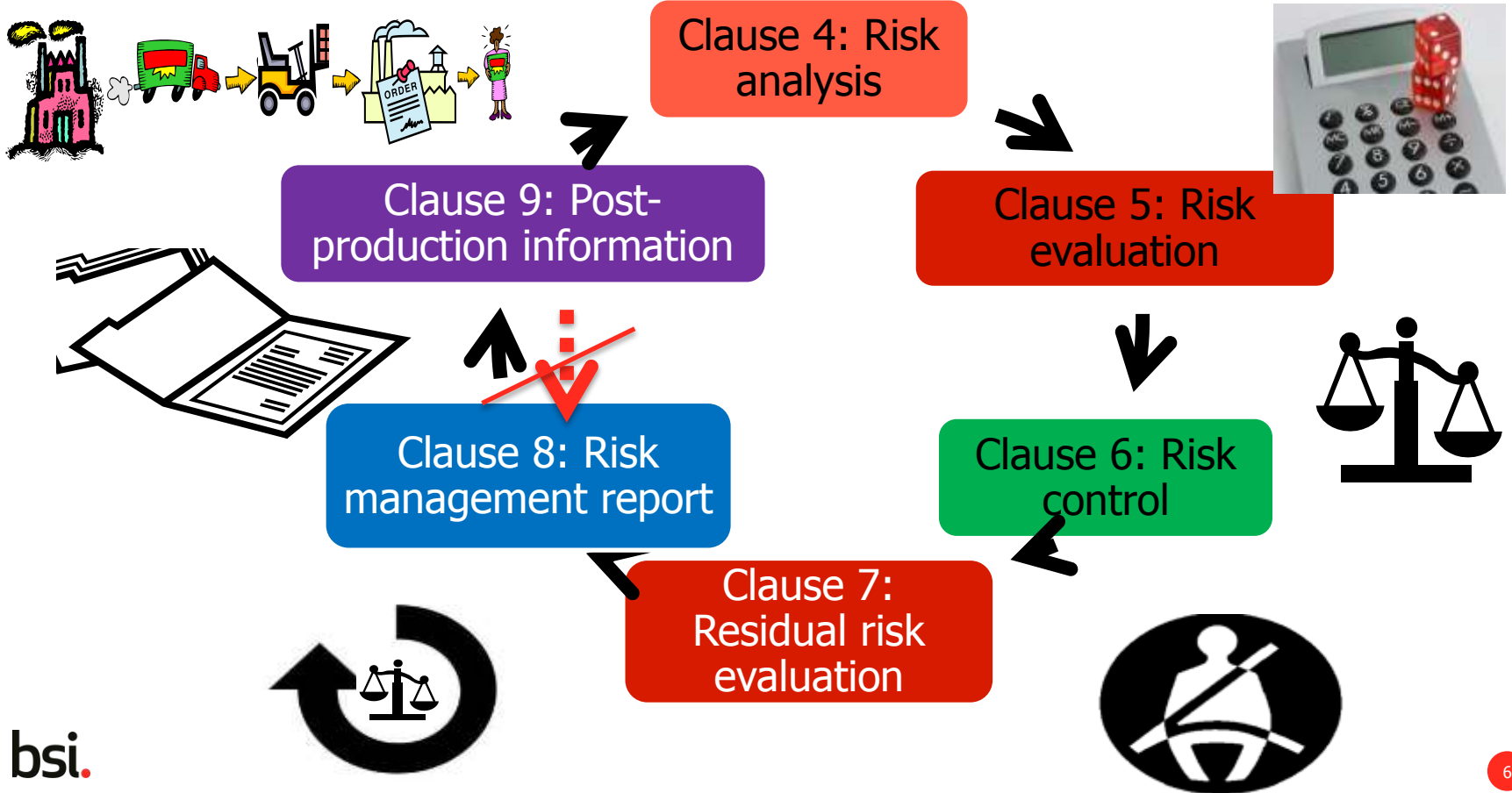
3.3 Qualification of personnel

3.4 Risk management plan

3.5 Risk management file

4. Annexes: A to J

# ISO 14971 – Main body (Clauses 4-9)

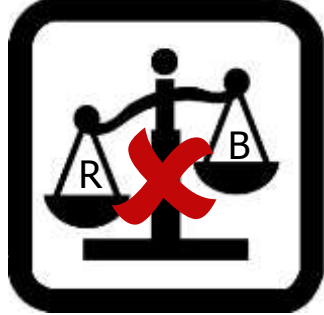


# Risk Management – EU Requirements



# Medical Devices – EU Risk Requirements

Risks > Benefits



Benefits > Risks





# The Directives – Where is 'Risk'?

	<b>MDD 93/42/EEC</b>	<b>AIMDD 90/385/EEC</b>	<b>IVDD 98/79/EC</b>
"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
<b>Total</b>	<b>41</b>	<b>18</b>	<b>24</b>

# EN ISO 14971:2012

- EU harmonized standard for Risk Management
- Allows the presumption of conformity to MDD, AMD, and IVD
- Published July 2012 & has replaced EN ISO 14971:2009

ISO	Reference	EN ISO 14971:2012	Date of publication	Date of cessation of presumption of conformity of superseded standard
ISO	14971:2009	14971:2012	30.8.2012	Note 1
CEN	EN ISO 14971:2009 (version 2007-10-01)	EN ISO 14971:2012	30.8.2012	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](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

# 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. <u>For content deviations, see points 1, 2, 3, 4 below.</u>

# **EN ISO 14971:2012**

## **– Content Deviations**



# EN ISO 14971:2012 – Content Deviations

Deviation	Essential Requirements (ERs) Impacted		
	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

MDD  
(AIMD)  
IVD



'...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).'

ISO 14971



'D.8.2 ...the manufacturer may discard negligible risks.'



# 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



'...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).'




ISO 14971



'5, 6.4, 6.5 & 7  
...manufacturers have the freedom to decide upon the threshold for risk acceptability.'

'D.6.1 ...only non-acceptable risks have to be integrated into the overall risk-benefit analysis.'

# Are all risks reduced as far as possible?

-  Unacceptable
-  Management Review Required - AI ARP
-  Broadly Acceptable

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

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

# Deviation No. 3

MDD  
AIMD  
IVD



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

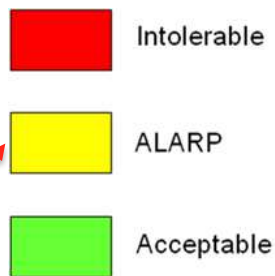
ISO 14971



'3.4 & D.8 ...contains the concept of reducing risks "as low as reasonably practicable."

The ALARP concept contains an element of economic consideration.'

# Are all risks reduced as far as possible?



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

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

# 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.

# Deviation No. 4

MDD  
AIMD  
(IVD)



....an overall risk-benefit analysis must take place in any case, regardless of the criteria established in the mgmt plan and requires undesirable side effects to "constitute an acceptable risk when weighed against the performance intended").'

ISO 14971



6.5 ...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 mgmt plan.

D.6.1 "A risk/benefit analysis is not required by this Int'l Std for every risk."

# The Directives – Where is 'Benefit'?

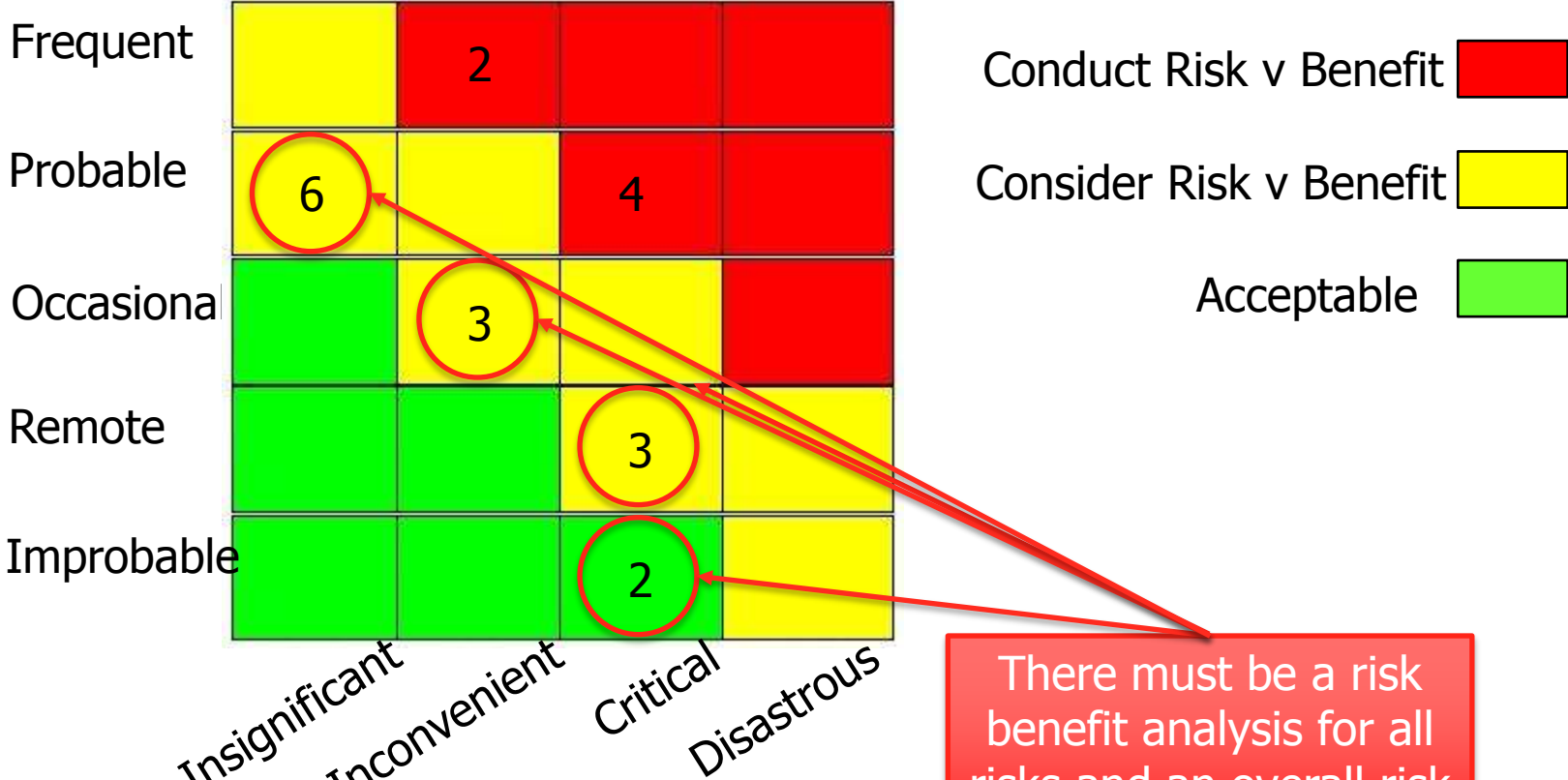
	<b>MDD 93/42/EEC</b>	<b>AIMDD 90/385/EEC</b>	<b>IVDD 98/79/EC</b>
"Benefit"	ERs: 1 7.4 11.2	ERs: 10	ERs: A – 1
<b>Total</b>	<b>3</b>	<b>1</b>	<b>1</b>

<b>"Risk"</b>	<b>41</b>	<b>18</b>	<b>24</b>
---------------	-----------	-----------	-----------

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



# Risk / benefit analysis done for all risks?



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

# Documentation of Risk / Benefit Analysis

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

# Deviation No. 5

...."to select the most appropriate solutions".....by applying *cumulatively* what has been called "control options" or "control mechanisms" in the standard.'

MDD  
IVD



ISO 14971



'6.2 ...oblige the mfr to "use one or more of the following risk control options in the priority order listed.'

'6.4 ...indicates that further risk control measures do not need to be taken if, after applying one of the options, the risk is judged acceptable according to the criteria of the risk mgmt plan.'

# 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

MDD  
IVD



ISO 14971



'... "eliminate or reduce risks as far as possible (inherently safe design and construction)".'

'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 . . ."  
without determining what is meant by this term.'

# 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

MDD  
IVD



...users shall be informed about the residual risks. This indicates that...the information given to the users does not reduce the (residual) risk any further.'

ISO 14971



'2.15 & 6.4 ...residual risk is defined as the risk remaining after application of risk control measures.'

'6.2 ...regards "information for safety" to be a control option.'

# 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.



# 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



**bsi.**

...making excellence a habit.™