

Balancing Risks Part 1 of 3



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Is your Quality Organization effectively balancing risks with opportunities ?

Are you assessing risk using the most appropriate tools ?

Are mind-traps biasing your assessment of risk ?

Agenda

The concept of risk.

Risk management
approaches expected by
ISO14971 (Medical Devices)

Management of Risk



What is risk
management ?





Purpose of risk management

- ❖ Purpose of risk management is to achieve safety.
- ❖ Performed to protect the patient, end-user and also compliance status.
- ❖ This unit will cover more broadly ways to balance risks with opportunities.



What is safety ?



What is the definition of safe ?

❖ Absence of **unacceptable** risk.

It isn't the absence of all risk, as zero risk is unattainable.

You have to decide what is an unacceptable risk v the benefit of an activity/ process / product.



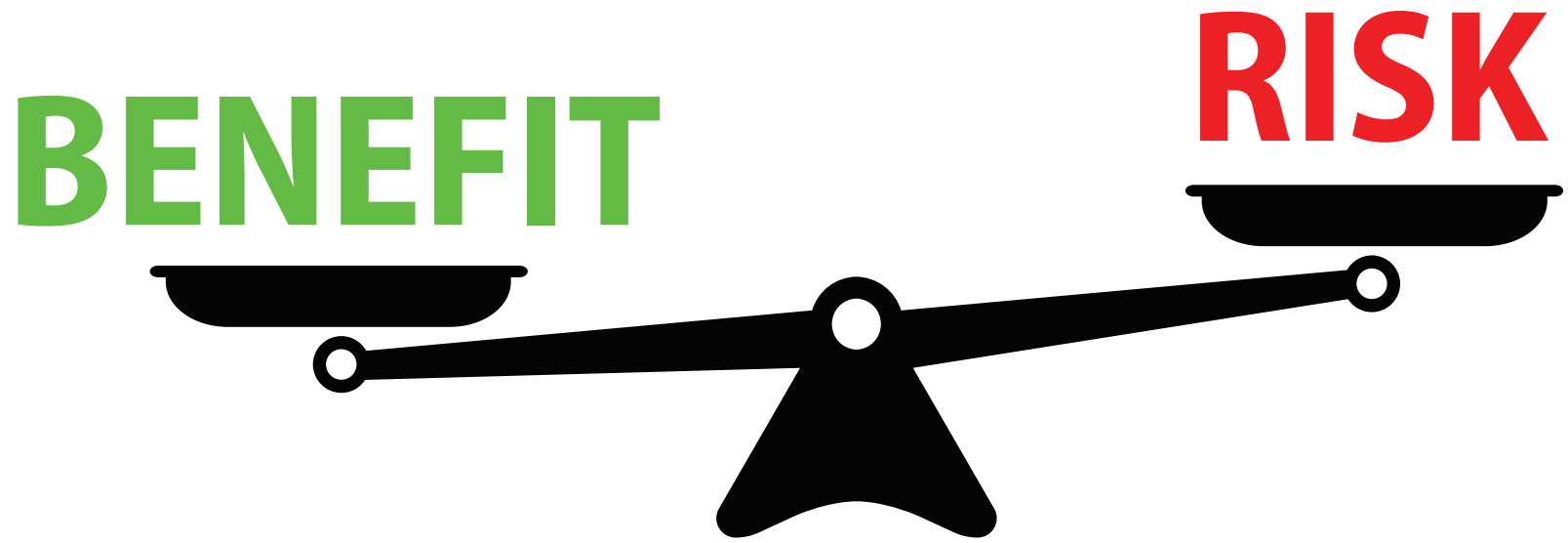
A collection of gaming peripherals is displayed on a dark surface. In the upper left, a mechanical keyboard with multi-colored backlit keys (red, blue, green, yellow) is visible. To its right is a black gaming mouse with a glowing red cord. In the lower right, a black Xbox-style game controller with glowing blue buttons is shown. In the lower left, a pair of black over-ear headphones with a glowing red headband lies on the surface. The entire scene is bathed in a mix of red, blue, and green light, creating a high-tech, gaming atmosphere.

What are the risks playing a
video game ?

A photograph of a crowded bar or restaurant interior. In the foreground, a man in a blue jacket and glasses is seated at a long bar, looking towards the camera. To his right, another man in a grey jacket is seen from the back. The bar is filled with people, some eating and some talking. In the background, a woman in a black uniform is standing near a counter. The bar has various signs, including one that says "EL PESCADO ORIGINAL" and another that says "MOZZARELLA ARTESANAL". There are also signs for "Salón Magerit Plaza" and "Moz heart". The lighting is warm and the atmosphere is busy.

What are the risks going into a crowded bar?

Risks v benefits



Covid pandemic

- Shielding
- Social distancing

Covid pandemic

- Social isolation
- Impact on schooling
- Access to primary healthcare

All risk management is a balance



Risk management is used:-

During product development. ISO 14971:2019

During post market surveillance.

During process or product changes.

During process validation.

During assessment of suppliers.

During assessment of deviations pre-product release ie: nonconformities.

What is risk ?

- ISO 13000:2018 Risk Management defines Risk as

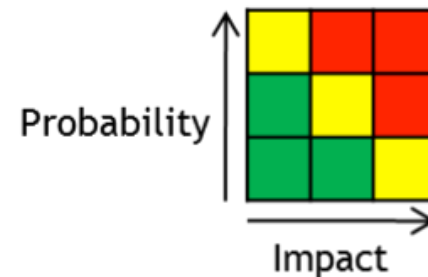
“effect of uncertainty on objectives”

It can be a positive or negative deviation from what is expected. It is a **goal** orientated view of risk. This is a relatively new way of looking at risk.

Traditional views see risk as a function of probability and impact.

This is an **event** orientated view of risk.

Both definitions can co-exist.



Standards, Directives and Regulations

- ❖ **ISO 14971: 2019** is the most recent standard on risk management for medical devices and replaces EN ISO 14971:2012. It currently describes state-of-the-art with respect to application of risk management for medical devices.
- ❖ **Directive 98/78/EC** on in vitro diagnostic medical devices point A.1 of Annex 1 covers risk management requirements and states:-
“Any risks which may be associated with their use must be acceptable when weighed against the benefits to the patient and be compatible with a high level of protection of health and safety. ”
- ❖ The in vitro diagnostic medical device regulations (**IVDR**) **2017/746** also cover regulatory requirements for risk management, for products marketed in the European Union. Under Chapter 1 / Annex 1. Point 3 states that:-

“ Manufacturers shall establish, implement, document and maintain a risk management system.

Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. ”

Key concepts in Risk Management

Probability

Hazard

Safe

Risk

Hazardous situation

Harm

State-of-the-art

Risk-Benefit

Risk assessment

Reasonable foreseeable misuse

Residual Risk

Overall Residual Risk

Risk evaluation

Risk analysis

Risk estimation

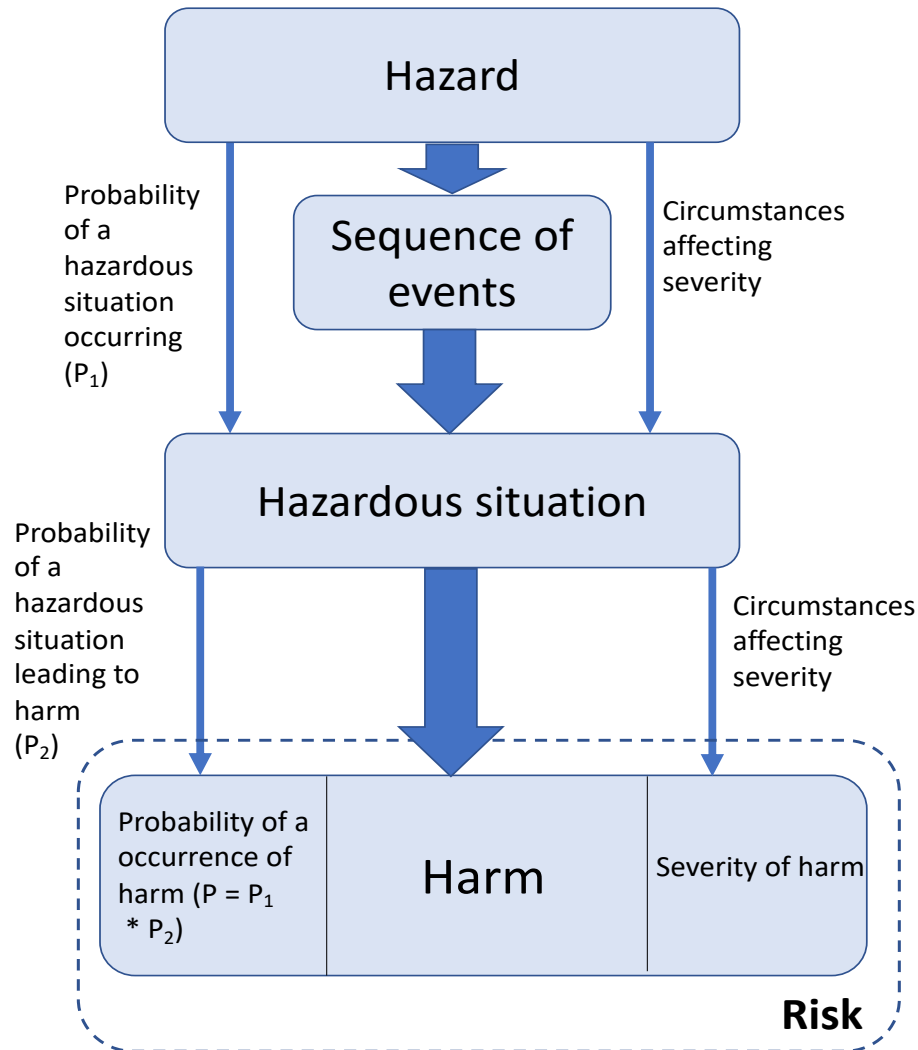
Risk control

Minimum reasonably acceptable risk

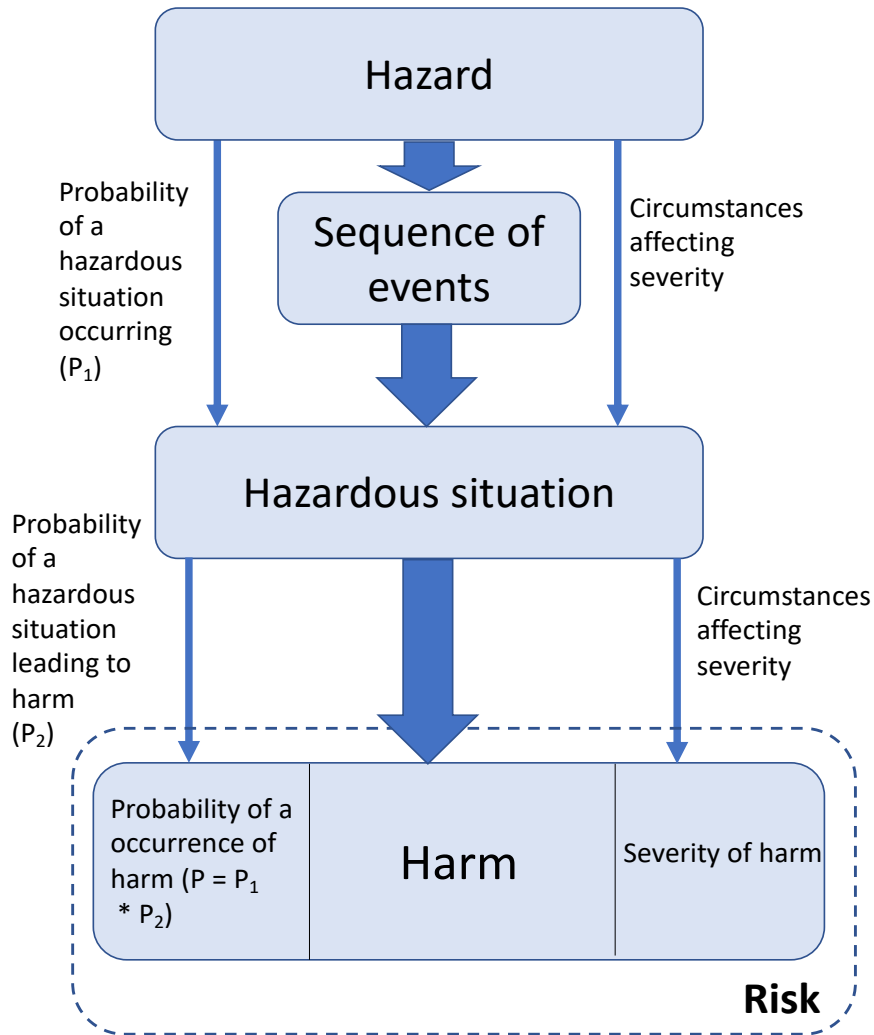
Benefit

Severity

Hazard, Sequence of events, Hazardous situation, Harm, Severity



Taken from ISO/IEC Guide 63: Guide to the development and inclusion of aspects of safety in International Standards for medical devices



Glass bottle



Bottle falls on ground and breaks





Broken glass



Cut feet



Other examples of hazard, hazardous situation and harm

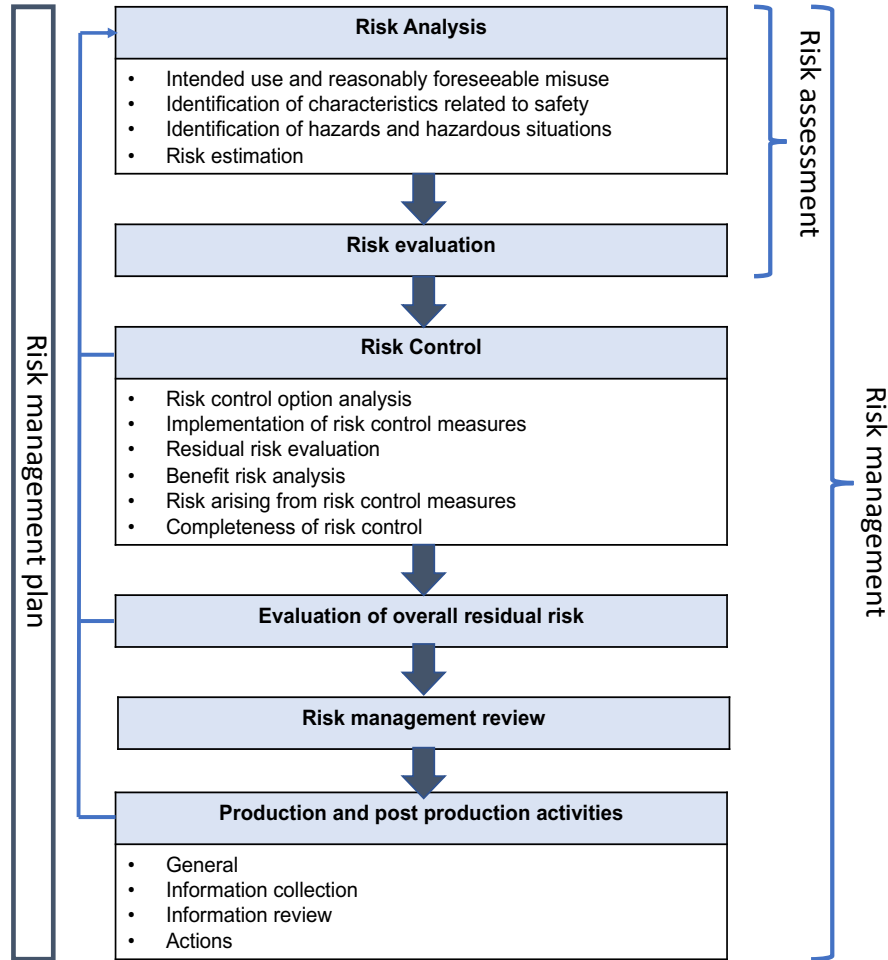
Hazard 	Lack of homogeneity in the batch	Accidental mechanical damage	Inadequate instructions in the IFU
Hazardous situation 	Unreliable results	Sharp surface	Use of diagnostic is unclear
Harm	Delay in treatment	Physical injury	Incorrect use of samples

Designating and Qualifying the Personnel Responsible

- ❖ A working team must be designated to perform the risk-management tasks for each product. This team must consist of personnel with knowledge of and experience with the product and its intended and unintended use, and knowledge of risk-management methods.
- ❖ A person responsible for coordinating all the work will be appointed.
- ❖ The working team will be composed of, but not limited, to representatives from **Medical Affairs**, R&D, Production, Quality Control, Regulatory and Quality Operations.



The risk management process: ISO 14971:2019



Risk Analysis =

Systematic use of available information in order to identify hazards and assess risks.

- An analysis of risk, based on the intended use of the diagnostic, and its reasonably predicted misuse should be performed and documented.
- The risk analysis of a similar diagnostic may be used as the basis of risk analysis of a new diagnostic. The design of the diagnostic being reviewed, individuals and function carrying out the review and the scope and date of the risk analysis should be documented.
- The intended use of the diagnostic will be documented. In addition, any reasonably foreseeable misuse should be documented.
- Any characteristics that could affect the safety of the diagnostic should be documented.
- All foreseeable hazards associated with the diagnostic based on its intended use and foreseeable misuse should be evaluated.



**Risk
Analysis**

Severity:

“ Measurement of the **possible consequences** of the hazard ”



RISK



- There is no separate Detection component.
- Detection is buried within the probability of harm component.

Probability of Occurrence of Harm

Level	Probability of Occurrence	Frequency
5	Frequent	Hazard occurs frequently. Would not be surprising if it occurred. ≥ 1 in 100 occasions.
4	Probable	Hazard occurs consistently at a low frequency. Would not be surprised if it occurred. < 1 in 100 and ≥ 1 in 1000
3	Possible	Hazard has the potential to occur. Would be surprised if it occurred. < 1 in 1000 and ≥ 1 in 10,000
2	Remote	Hazard has the potential to occur. Would be surprised if it occurred. < 1 in 10,000 and ≥ 1 in 100,000
1	Improbable	Hazard has an extremely remote potential to occur. Would be surprised if it occurred. < 1 in 1,000,000

Manufacturers needs to develop their own Probability of Occurrence of Harm scale.

This is an example.

Probability Estimation

- Often the data won't be available to make an accurate assessment of probability of occurrence of harm.
- Use historical data from similar diagnostics if possible.
- Err on the side of caution.
- Base your probability estimate on the presumption you will implement no control measures yet.

$y = g(x)$
Secant Lines

$$f'(x) = \lim_{h \rightarrow 0} \frac{f(x+h) - f(x)}{h}$$

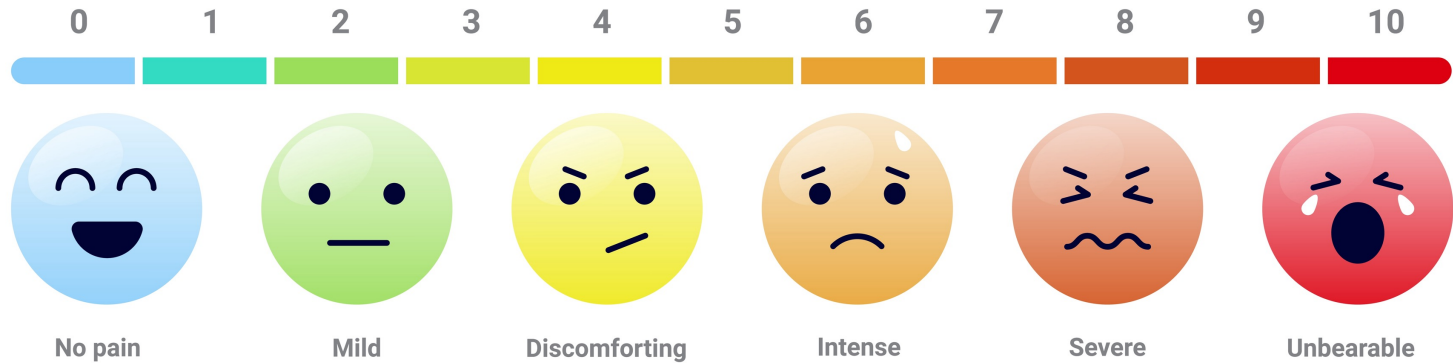
$$f(x) = \lim_{h \rightarrow 0} \frac{(x+h)^2 - x^2}{h}$$

$$= \lim_{h \rightarrow 0} \frac{x^2 + 2xh + h^2 - x^2}{h}$$

$$= \lim_{h \rightarrow 0} \frac{2xh + h^2}{h}$$

$$g(x+h) - g(x) = \lim_{h \rightarrow 0} h(2x + h)$$

Severity



Manufacturers needs to develop their own Severity scale.

This is an example.

Level	Severity	Impact
5	Catastrophic	Harm to patient/user: requires emergency surgery. May cause permanent injury or death.
4	Critical	Harm to patient/user: requires medical or surgical intervention.
3	Major	Harm to patient/user: able to be cured with minor treatment.
2	Minor	Potential for harm to the patient/user.
1	Negligible	No potential for harm to the patient/user. Inconvenience.

Severity

Remember Severity is:

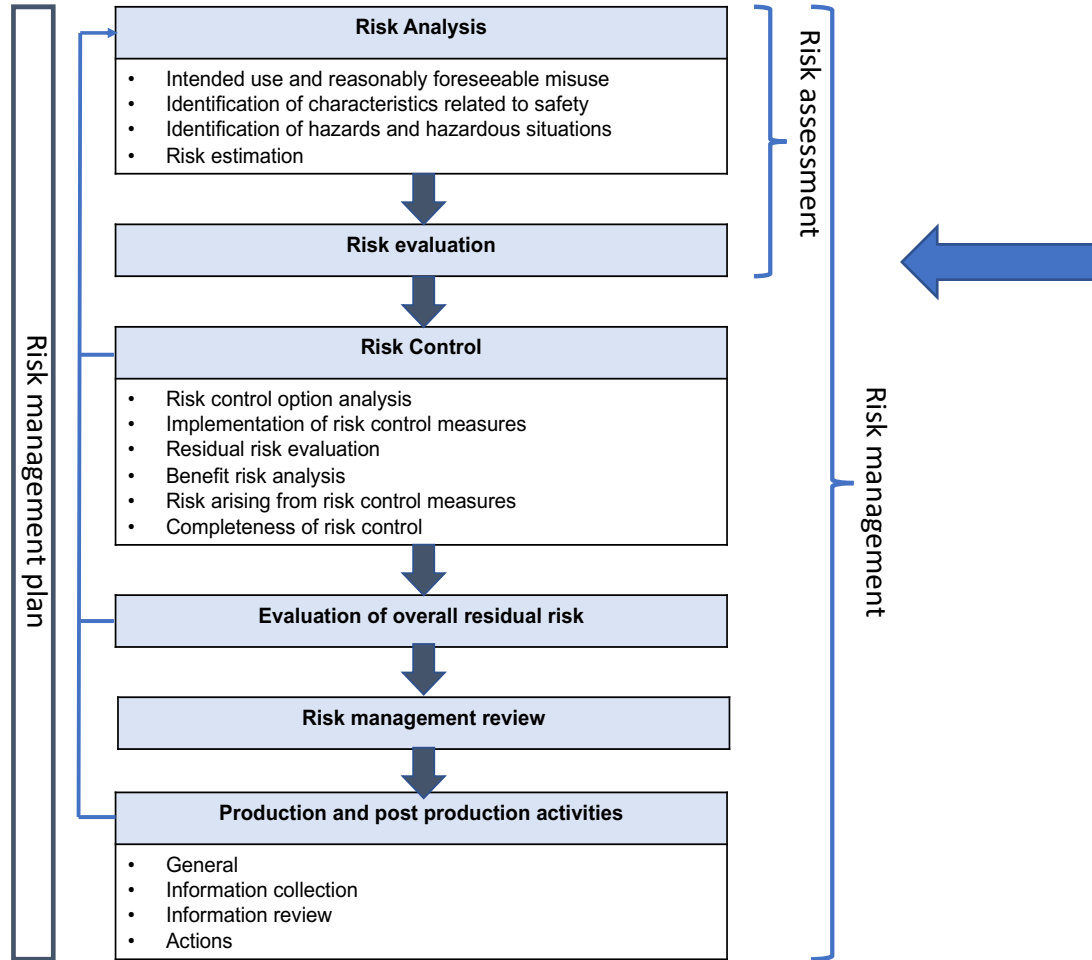
“Measurement of the **possible** consequences of the hazard”

Base severity on the presumption that the occurrence of harm has happened or will happen.

These consequences need to be **realistic**.



The risk management process: ISO 14971:2019



Risk Evaluation

- Risk Evaluation =**
 Process of comparing estimated risk against risk criteria to determine acceptability of risk.

Each manufacturer needs to determine the level of risk acceptability.

Often risk is stratified into three bands, low to high.

Probability of Harm						
Frequent	5	Unacceptable	Unacceptable	Unacceptable	Unacceptable	Unacceptable
Probable	4	Undesirable	Undesirable	Unacceptable	Unacceptable	Unacceptable
Possible	3	Acceptable	Undesirable	Undesirable	Unacceptable	Unacceptable
Remote	2	Acceptable	Acceptable	Undesirable	Undesirable	Unacceptable
Improbable	1	Acceptable	Acceptable	Acceptable	Undesirable	Undesirable
Severity		1	2	3	4	5
		Negligible	Minor	Major	Critical	Catastrophic





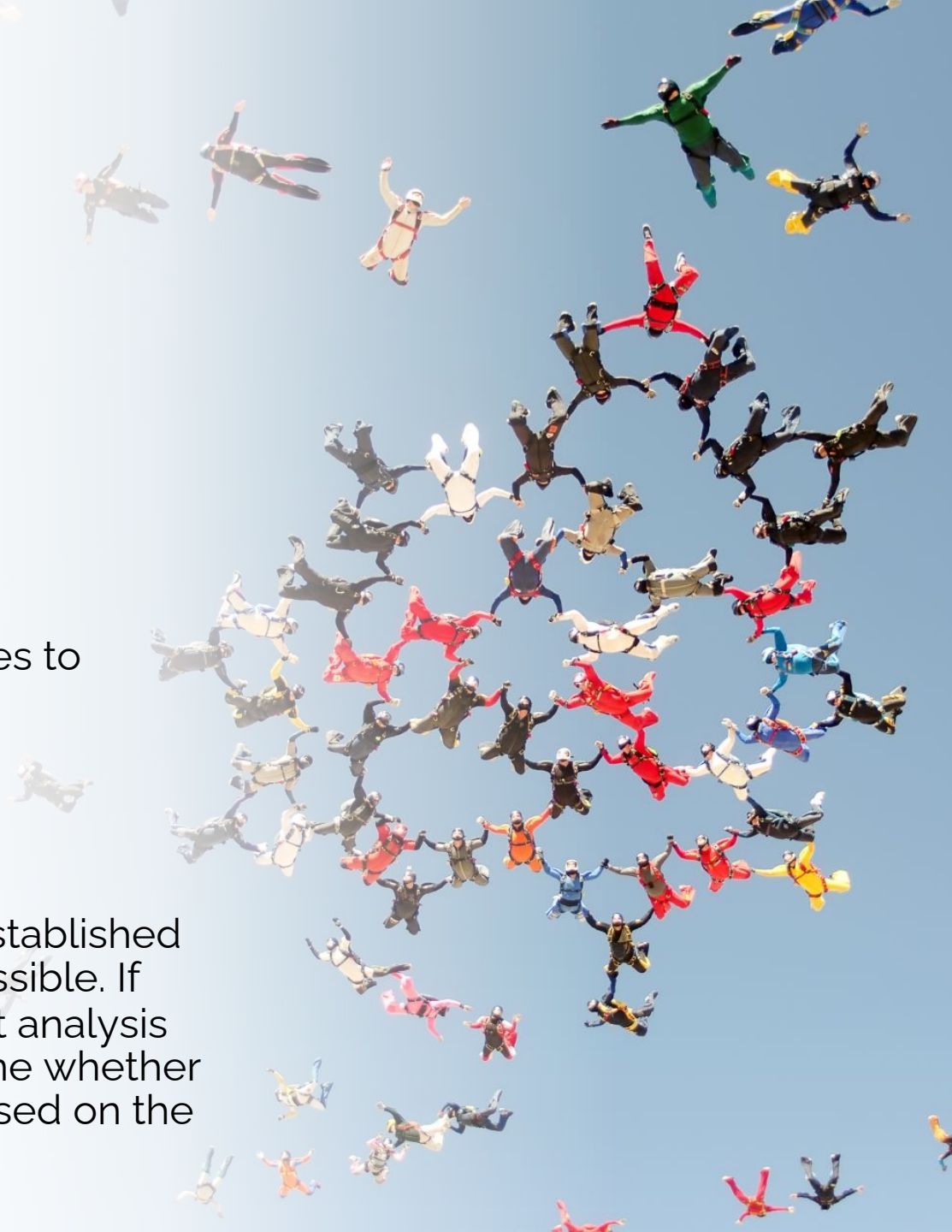
Unacceptable and Undesirable Risks

Unacceptable Risks

➤ Unacceptable risks require the establishment of control measures to reduce the level of risk.

Undesirable Risks

➤ Control measures should be established for Undesirable risks as far as possible. If this is not possible a risk – benefit analysis should be performed to determine whether the residual risk is acceptable based on the benefit of the diagnostic.



Acceptable Risks

Do I have to implement control measures ?

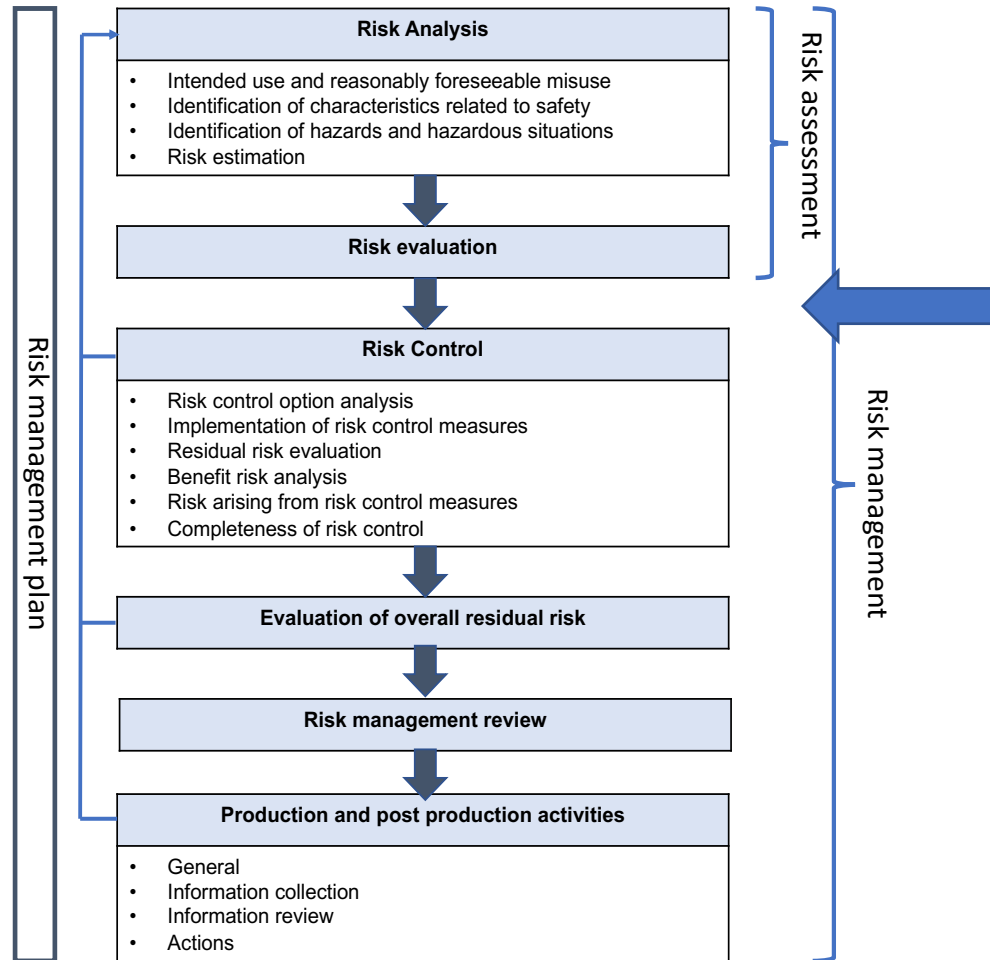
- **ISO14971: 2019**

" If the risk is acceptable, it is not required to apply the requirements given in 7.1. to 7.5 [risk control] to this hazardous situation "

- **(IVDR) 2017/746 In vitro Diagnostic Regulations**

- *" All known and foreseeable risks, and any undesirable effects shall be **minimised** "*

The risk management process: ISO 14971:2019



Risk Control

Risk control measures will be applied to reduce the risks to an acceptable level. The following should be applied in order of priority as described in ISO14971:2019 Section 7 (Risk Control).



Risk Control

1: Inherently safe by design and manufacture



For all the failure modes identified the risk is reduced principally through implementation of controls that ensure the device is inherently safe by design and manufacture following the expectations of ISO14971:2019.



Firstly, the device is ensured safe by implementation of appropriate design controls as defined in ISO13485:2016 to ensure that the modified device fulfils design requirements and all customer and regulatory expectations.

Secondly, consistent and safe manufacture is ensured through the execution of an effective Quality Management System (QMS) to ensure that risks are reduced.

Risk Control

2: Protective measures



Protective measures in the medical device itself or in the manufacturing process to detect failures.



Alarms.
Control systems during manufacturing.
Product inspection.
Release tests etc.

Risk Control

3: Information and training



Control measures that increase awareness of potential failures from occurring through use of the device.



- Instructions for Use
- Warnings
- Labelling
- Operator training and required competency

Acceptable Risk

- After control measures have been implemented the residual risk will be evaluated using the criteria described above. If the residual risk is still deemed not acceptable, further control measures will be considered.
- If the residual risk is still deemed Undesirable and further risk controls are not practical, for each risk a determination will be made whether the benefit of the diagnostic outweighs the residual risk.
- If the benefit outweighs the risk this risk level will be determined as acceptable risk.

- ❖ The assessment of the residual risks should be documented. This is an example.
- ❖ List all the control measures for each risk.

#	☑	Hazard	Hazardous Situation	Cause	Harm	P	S	Initial Risk Band	Control methods / Verification	P	S	Residual Risk Band	Benefit over risk ?
1	Y	Device not specific / sensitive for IgG antibodies.	Device with poor specificity or sensitivity used with patient samples.	Incorrect design of device.	Erroneous results. Delay in medical decision.	4	3	Unacceptable	<ul style="list-style-type: none"> Supplier controls to ensure raw materials sourced meet requirements. Application of appropriate design controls to ensure device meets requirements of sensitivity and specificity. Performance verified through clinical tests during product development to ensure required specificity and sensitivity. 	1	3	Acceptable	Y

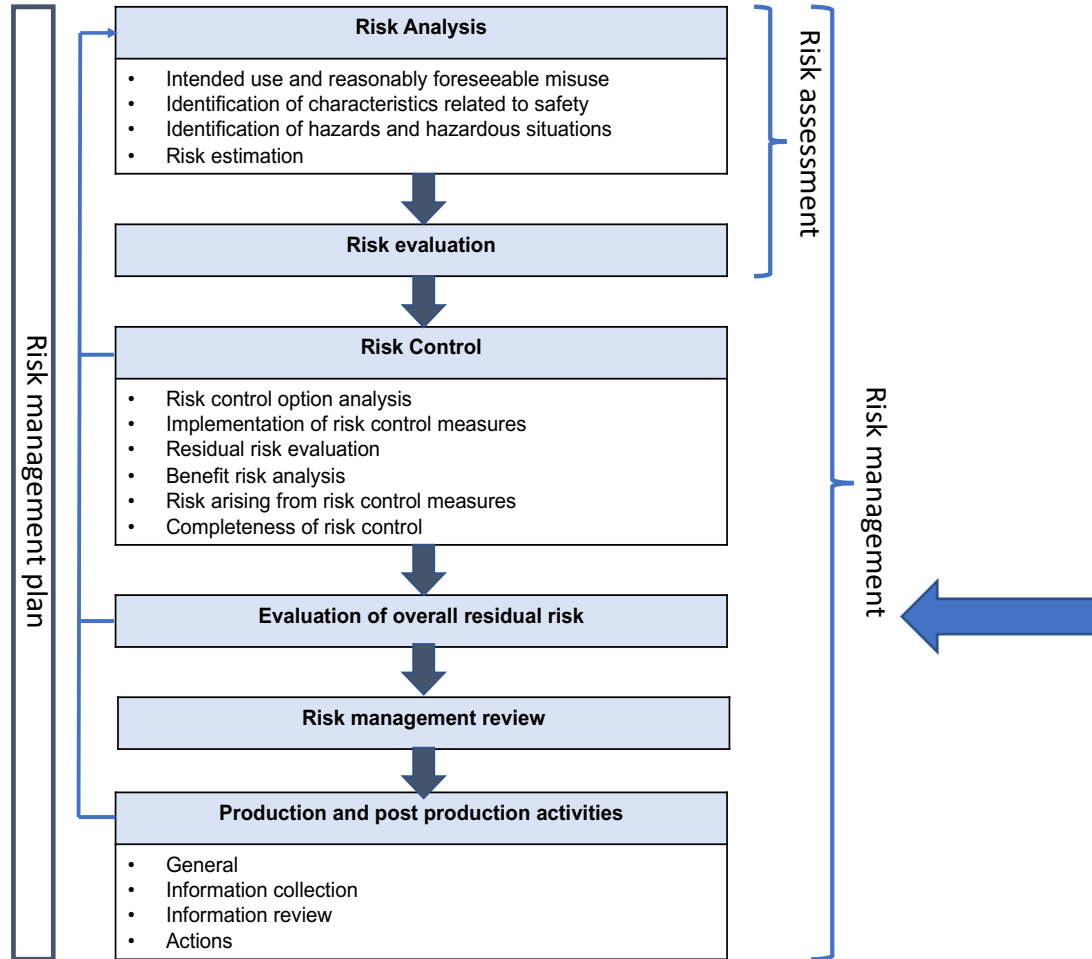
- ❖ A review of the risk control measures should be carried out and documented to determine whether as part of the process, new hazards have been introduced or the risk level of previous hazards have increased. In addition, the completeness of all the risk control measures should be evaluated and documented.

Items to consider when completing a risk assessment template include:

- Be careful when documenting any required mitigations that they are proportionate to the risk.
- You will need to demonstrate implementation of these actions.
- Ensure that you have the resources, time, and effort available to deliver them. Mitigations that are downgraded – through your inability to execute them - seriously impact your commitment to the risk management process and will be frowned on during regulatory inspection.

- Ensure that you have the needed competencies to complete the document.
- This is particularly relevant for any expertise covering how the customer uses your product, ie: a clinician if it is a medical device.
- Do not second guess how your customer uses the product. Ideally involve them in the process.
- Agree beforehand how decisions will be made with respect to scoring of risk and proposed mitigation activities.

The risk management process: ISO 14971:2019



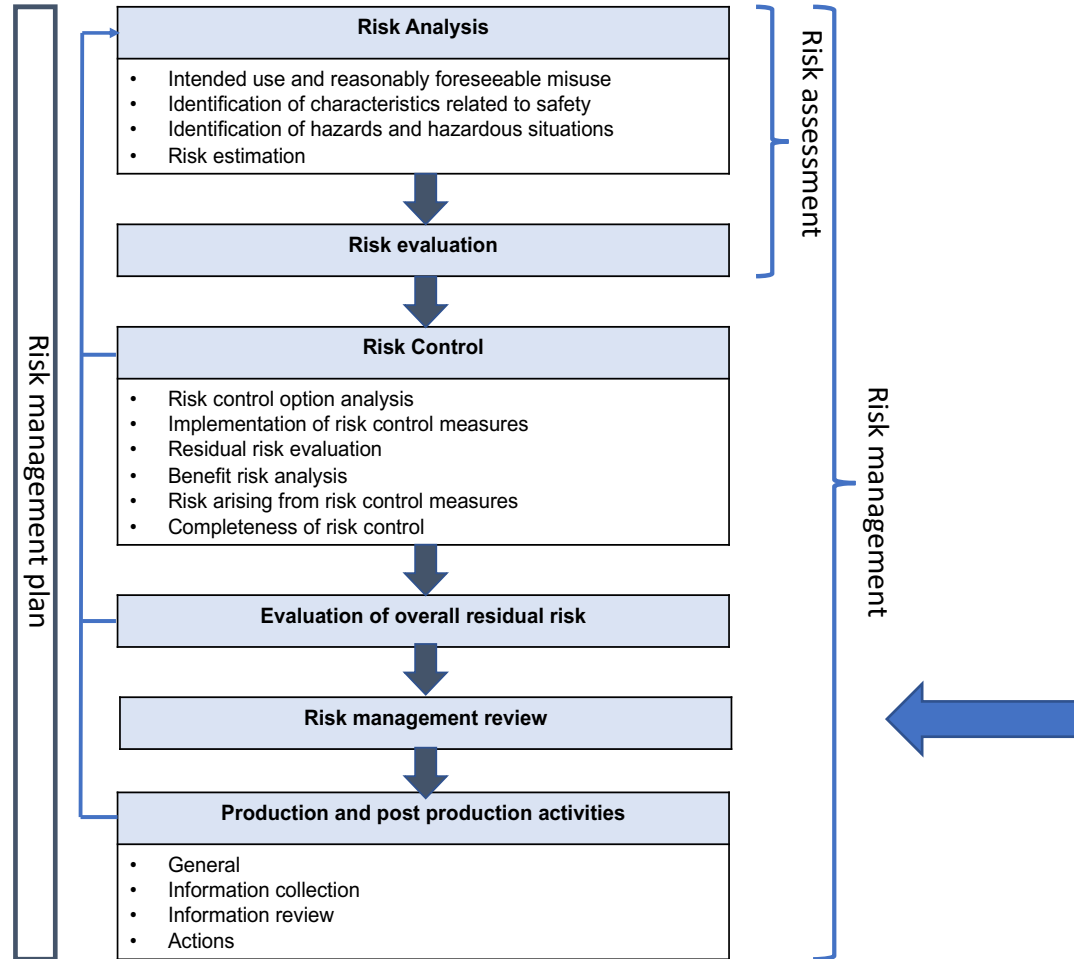
Evaluation of overall residual risk

- ❖ In addition to the individual risks being assessed for acceptability, the Overall Residual Risk should be assessed to determine whether, though individual risks themselves may be deemed acceptable, collectively they are deemed not acceptable. The Overall Residual Risk will be documented.
- ❖ This is an assessment of all the combined individual risks and the methodology to calculate this needs to be defined. ISO14971: 2019 gives limited / no guidance on how to calculate this Overall residual Risk.

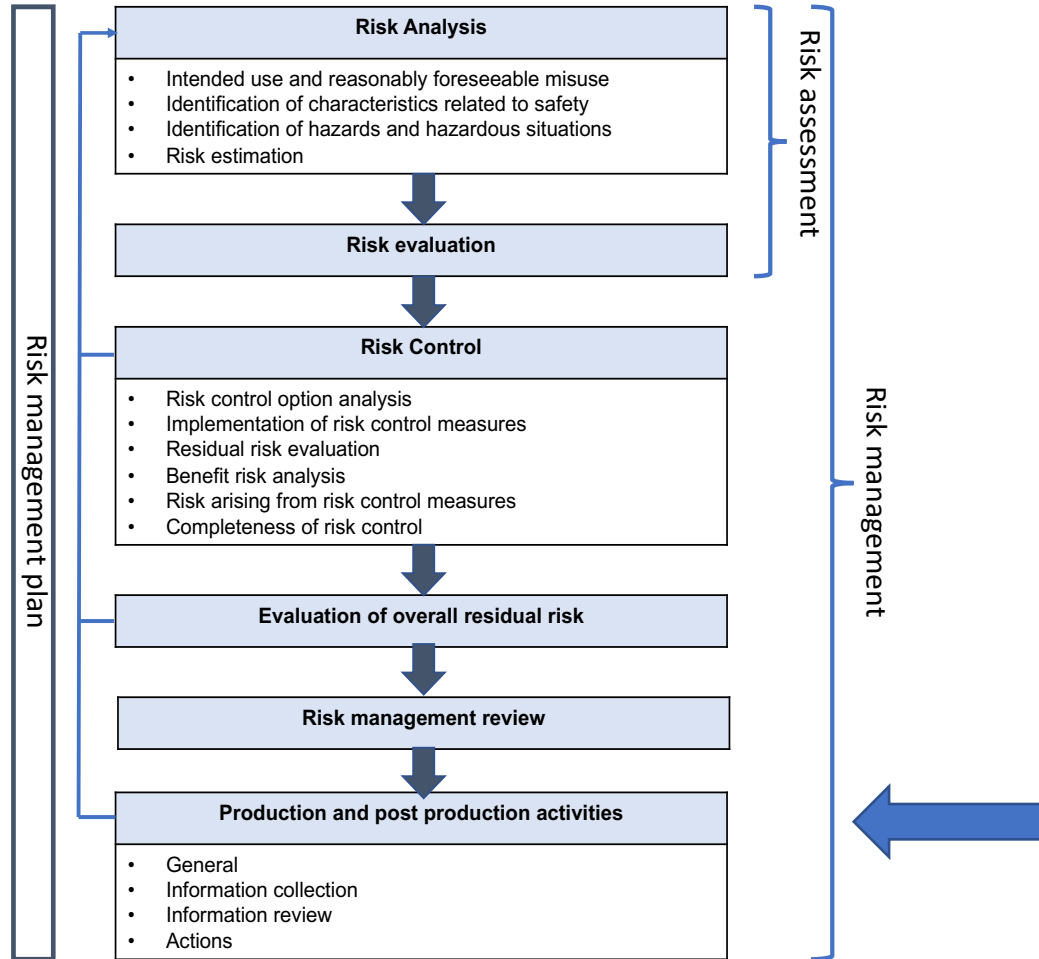
Evaluation of Overall Residual Risk

- ❖ One way of assessing the Overall Residual Risk is via “Expert Panel”.
- ❖ On review of the individual residual risks, an Expert Panel can determine the Overall Residual Risk based on technical knowledge of the diagnostic, knowledge of the control measures implemented and the use of the diagnostic in the clinical setting. An assessment should be made of whether the benefits of the diagnostic outweighs the Overall Residual Risk. This assessment will be documented.
- ❖ The Expert Panel should comprise of representatives from the following functions: R&D, Quality, Operations and Medical Affairs.

The risk management process: ISO 14971:2019



The risk management process: ISO 14971:2019



Production and post production activities

- ❖ Risk management is an iterative closed loop process and risk should be continually evaluated based on – but not limited to – use of the diagnostic in the field; state-of-the-art; performance of similar devices; production and supply chain performance; implementation of corrective or preventive action; revised standards or any other relevant information in the public domain.
- ❖ The information should be reviewed to determine whether unrecognised hazards are present; the estimated individual risks are no longer acceptable; the Overall Residual Risk is no longer acceptable or whether the state-of-the-art has changed.

Production and post production activities

- ❖ The effectiveness of the risk-control methods should be assessed at intervals based on feedback from internal (non-conformances) and external (complaints) sources.
- ❖ In addition to the above the suitability of the risk management process should be assessed by management as part of the Quality Management System review process.

COMPLAINTS

