Regulatory, quality and clinical affairs

NX-451 – What to know when working with medical devices

Session 6

Kim Rochat

last update 2025-03-27

Risk Management – applicable guidance

ISO 14971 - Medical devices — Application of risk management to medical devices

5.4 Identification of *hazards* and *hazardous situations*

The *manufacturer* shall identify and document known and foreseeable *hazards* associated with the *medical device* based on the *intended use*, *reasonably foreseeable misuse* and the characteristics related to *safety* in both normal and fault conditions.

For each identified *hazard*, the *manufacturer* shall consider the reasonably foreseeable sequences or combinations of events that can result in a *hazardous situation*, and shall identify and document the resulting *hazardous situation(s)*.

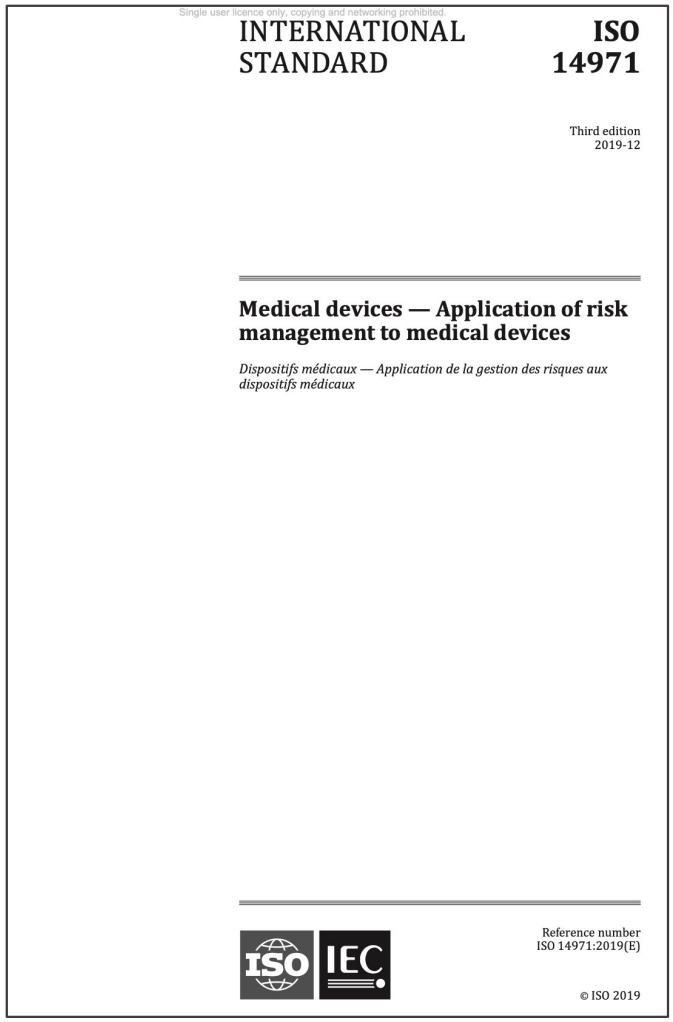
5.5 *Risk estimation*

For each identified *hazardous situation*, the *manufacturer* shall estimate the associated *risk(s)* using available information or data. For *hazardous situations* for which the probability of the occurrence of *harm* cannot be estimated, the possible consequences shall be listed for use in *risk evaluation* and *risk control*. The results of these activities shall be recorded in the *risk management file*.

The system used for qualitative or quantitative categorization of probability of occurrence of *harm* and *severity* of *harm* shall be recorded in the *risk management file*.

6 *Risk evaluation*

For each identified *hazardous situation*, the *manufacturer* shall evaluate the estimated *risks* and determine if the *risk* is acceptable or not, using the criteria for *risk* acceptability defined in the *risk management* plan.



INTERNATIONAL STANDARD

ISO 14971

Third edition
2019-12

Medical devices — Application of risk management to medical devices

Dispositifs médicaux — Application de la gestion des risques aux dispositifs médicaux

Reference number
ISO 14971:2019(E)

Risk Management – Risk analysis method

Risk = ***probability of occurrence (P)*** *of harm x* ***severity (S)*** *of that harm*

Hazard: sharp blade

Hazardous Situation: attach blade to holder

Harm: patient is cut

Risk = P_1 X P_2 X Severity

P_1 *is probability of hazardous situation occurring*

P_2 *is probability of hazardous situation leading to harm*

Often P is used which integrates directly $P_1 x P_2$

Risk Management – Risk analysis concept

Definition of probability and severity scale for my risk analysis

Severity Level	Factor (score)
Negligible	1
Minor	2
Serious	3
Critical	4
Catastrophic	5

Probability Level	Quantitative Probability
Improbable	1
Remote	2
Occasional	3
Probable	4
Frequent	5

Risk = Probability X Severity

Risk Management – Risk analysis concept

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Risk = Probability X Severity

	Severity (S)				
Probability of Occurrence (O)	Very Low (1)	Low (2)	Moderate (3)	High (4)	Very high (5)
Improbable (1)	1	2	3	4	5
Remote (2)	2	4	6	8	10
Occasional (3)	3	6	9	12	15
Probable (4)	4	8	12	16	20
Frequent (5)	5	10	15	20	25

⇒ **frequent risk with a moderate severity = Level of 15**

Risk Management – Risk analysis concept

Definition of risk acceptability

Risk Level	Common Terms	Interpretation
RL ≥ 10	Unacceptable risk	Risks too severe to be accepted. A risk above this limit shall be reduced through mitigation measure(s) or risk control(s).
10 > RL > 4	Significant risk	The risks in this range are deemed acceptable, only if the reduction is not technically possible. If the risk may be reduced, then a mitigation measure or a risk control shall be implemented. Risk can be acceptable only with a favourable Risk/Benefit ratio.
4 ≥ RL	Acceptable risk	Risk is acceptable. It represents the low-risk area where a mitigation measure would not result in significant risk reduction. When this level is achieved during initial evaluation, if possible, it should be further mitigated. This status is when the risk is reduced As Far As possible

Example of risk acceptability level

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Risk Management – Risk analysis concept

Risk evaluation

Risk Identification				Initial risk level		
ID #	Cause / Failure Mode	Hazardous situation / effect(s) of failure	Harm / Damage	S	P	Score
1	The glue selected for the medical adhesive is not biocompatible	The glue is absorbed by the skin provoking an allergic reaction	Mild skin irritation	2	4	8
2	Battery of the external defibrillator is not certified for the define used	The battery explode when defibrillator at maximum power	Sever injury to patient and medical personnel	5	3	15

⇒ My risk 1 has a level of 8, it is a significant risk

⇒ My risk 2 has a level of 15, it is unacceptable

Risk Management – Risk control

Once risks are identified and estimated, the manufacturer shall reduce them **as far as possible**.

The objective is to define measures that can be implemented which by themselves reduced the identified risk.

There is mainly two ways to reduce a risk level:

1) Implementing a measure that reduce the probability of occurrence of a risk
2) Implementing a measure that reduce the severity of the harm

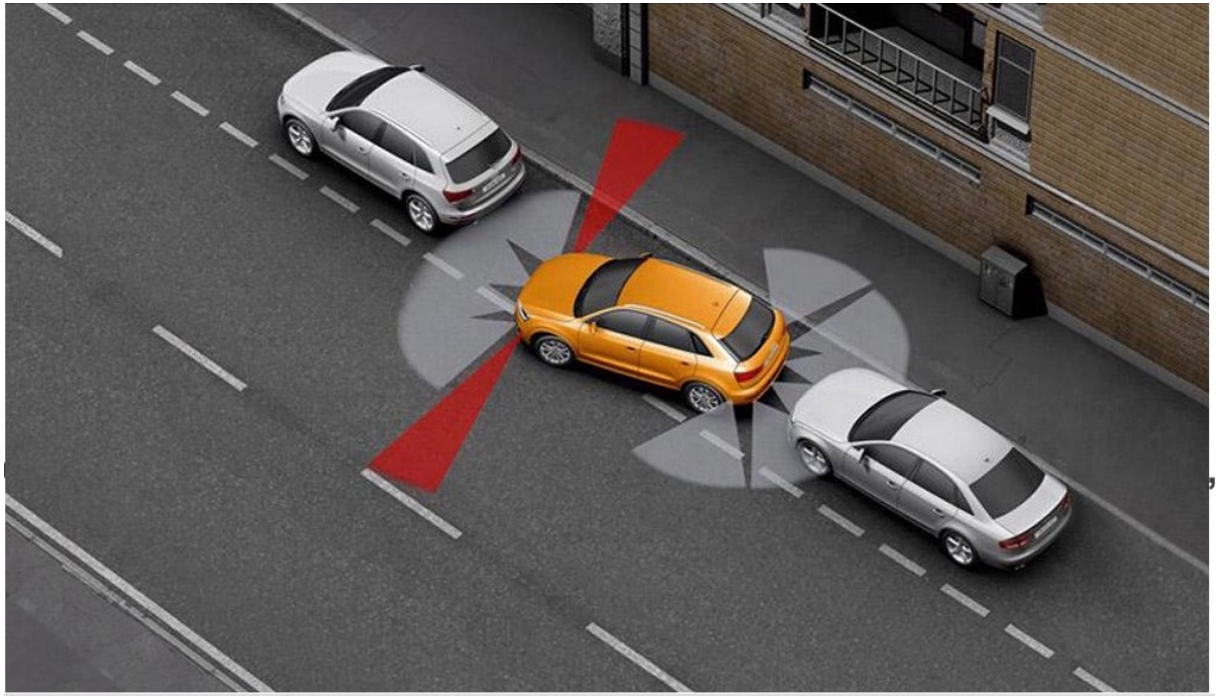
Risk Management – Risk control

Reduction of the impact of the harm

The airbag does not reduce the likelihood of a car accident occurring, but if an accident happens, it helps reduce the impact on the passenger.

Risk Management – Risk control

Reduction of the probability of occurrence



Parking assistance does not reduce the damage if your car hits a wall, but it helps prevent such incidents from happening.

Risk Management – Risk control

Risk treatment

Risk Identification				Initial risk level		
ID #	Cause / Failure Mode	Hazardous situation / effect(s) of failure	Harm / Damage	S	P	Score
1	The glue selected for the medical adhesive is not biocompatible	The glue is absorbed by the skin provoking an allergic reaction	Mild skin irritation	2	4	8

Treatment plan (Mitigation)				Initial risk level		
ID #	Risk control / mitigation measure description	Additional risk	Evidence of Implementation	S	P	Score
1	The glue selected shall be biocompatible according to 10993	The new glue does not support prolonged contact with water	REQ-123	2	1	2

Outcome:
1) The initial risk is now acceptable (RL =2)
2) We have an additional risk to consider
3) We have adjusted the requirement for traceability (REQ-123)

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Risk Management – Risk control

Risk mitigation outcome

1) We have an additional risk to consider

Risk Identification				Initial risk level		
ID #	Cause / Failure Mode	Hazardous situation / effect(s) of failure	Harm / Damage	S	P	Score
2	The selected glue for the medical adhesive does not support prolonged contact with water	The medical adhesive may come off in case of patient bath or shower while still need to protect the skin	Medical adhesive need to be replaced with a new adhesive	1	4	4

2) We have to update the requirement

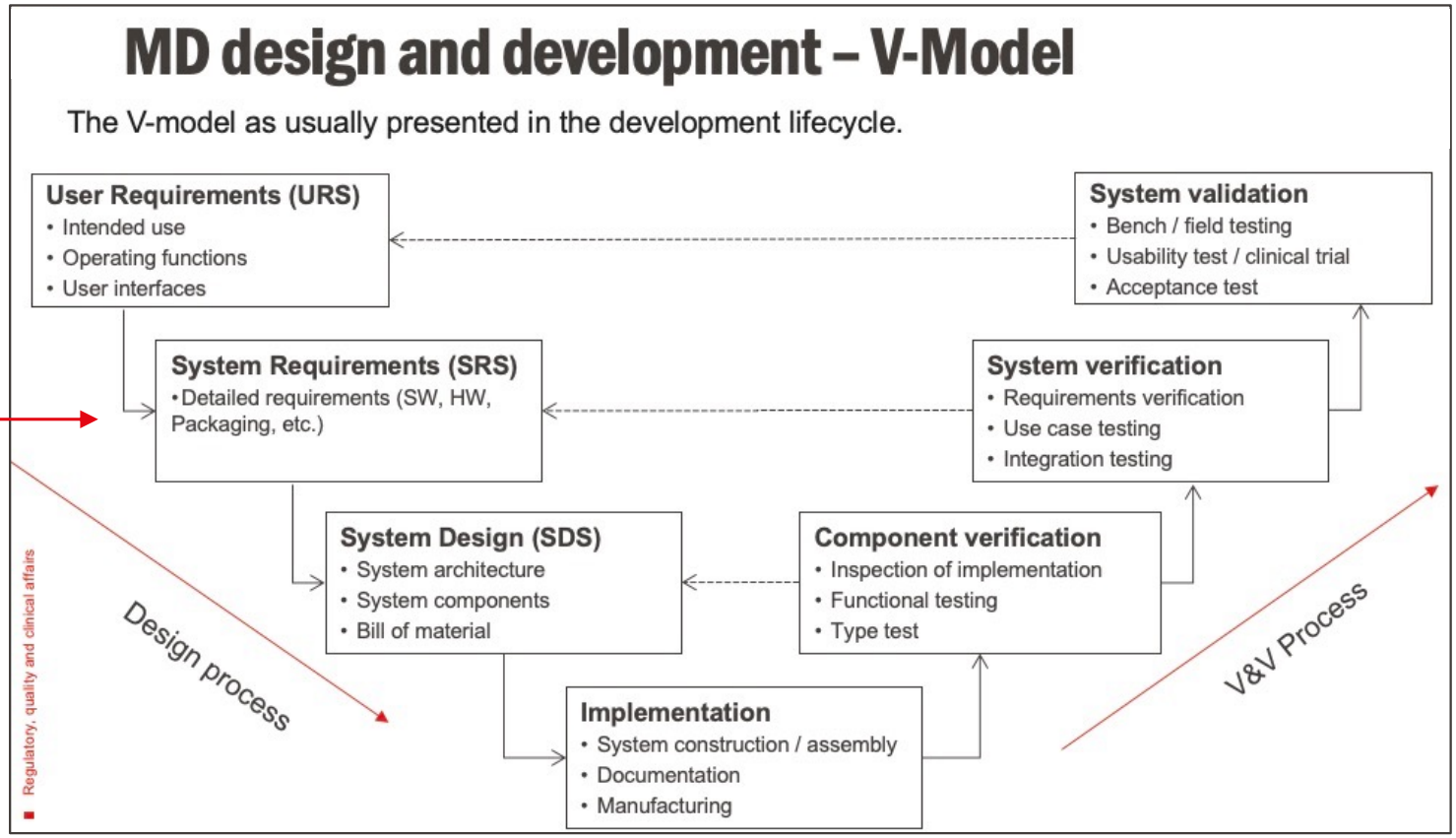
Medical adhesive glue - REQ-123 / shall

The selected glue used for the medical adhesive shall be biocompatible according to IEC 10993. A declaration of conformity shall be provided

Risk Management – Risk control

Update requirements

Medical adhesive glue - REQ-123 / shall



Slide 8 – session 4

Risk Management – Risk control

Nature of controls

Risk control measures adopted by manufacturers for the design and manufacture of the devices shall conform to safety principles, taking account of the generally acknowledged state of the art. To reduce risks, Manufacturers shall manage risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers shall, in the following order of priority:

(a) eliminate or reduce risks as far as possible through safe design and manufacture;

(b) where appropriate, take adequate protection measures, including alarms if necessary, in relation to risks that cannot be eliminated; and

(c) provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users.

Manufacturers shall inform users of any residual risks.

Risk Management – Risk control

Nature of controls

Clause 7.1 of ISO 14971 provide specific requirements for the definition of risk control: "*The manufacturer shall use one or more of the following risk control options in the priority order listed:*

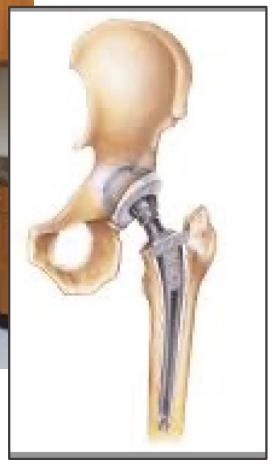
- *inherently safe design and manufacture;*
- *protective measures in the medical device itself or in the manufacturing process;*
- *information for safety and, where appropriate, training to users."*

There is an ongoing debate on whether informing or training the users contributes to reduce severity of probability of a risk. Thus, the standards consider them as relevant risk controls

Risk Management – Risk control

Nature of controls - inherently safe

On a lancet, the needle automatically retracts after injection, to prevent needlestick injuries or cross contamination



Some medical implants (e.g., pacemakers, orthopedic implants) are made from non-magnetic materials (e.g., titanium instead of steel) to reduce the risk of interactions with MRI machines (MR Safe)

Risk Management – Risk control

Nature of controls - protective measures

Medical drills are equipped with a speed controller that automatically cuts the current to the motor if the rotational speed exceeds the predefined safety limit, preventing potential tissue damage and ensuring precise surgical performance.

⇒ It monitors the motor speed and reacts when a hazardous situation occurs (excess speed).

The emergency stop button on an MRI machine allows the operator to immediately halt the scan if there is a safety concern, such as patient discomfort, equipment malfunction, or the presence of metallic objects in the magnetic field.

⇒ It doesn't prevent the hazard but mitigates its consequences by allowing intervention to stop it.

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Risk Management – Risk control

Nature of controls - information for safety

6. Fit your Aktiia bracelet on your wrist.

⚠	**Follow the Aktiia app on-screen instructions or carefully read the instructions in the "Correct Aktiia bracelet positioning" section (§12) of this user manual.**

7. Fit your Aktiia cuff on the opposite arm.

Follow the on-screen instructions, noting the Aktiia cuff must be placed on the opposite arm as the Aktiia bracelet, i.e., if you wear the Aktiia bracelet on your RIGHT wrist, place the Aktiia cuff over your LEFT arm and vice versa.

⚠	**The accuracy of blood pressure measurement done by Aktiia Cuff depends on the correct Cuff positioning. Please carefully read the instructions in the section "Correct Aktiia Cuff positioning" (§13) of this user manual.**

8. Initialize your Aktiia bracelet.

In the Aktiia app, carefully follow the instructions to complete the initialization procedure. The Aktiia cuff will start inflating.

9. Switch OFF your Aktiia cuff.

⚠	**The accuracy of the initialization process depends on your body posture during the initialization. Carefully read the section "Body Posture during Initialization Procedure" (§14) of this user manual.**

Congratulations! Your Aktiia bracelet is now initialized and ready to track your blood pressure!

⚠	**You need to complete an initialization procedure at least once per month, or when prompted by the mobile application. Data obtained outside the initialization period may be inaccurate.**

Caution

Information for safety are provided in the instruction for use (IFU) or on the labelling. It is usually provided in the form of «Warnings» or «Caution». Alarms and warning messages (i.e. on a screen) are also considered as Information for safety.

Source: https://aktiia.com/ch/wp-content/uploads/sites/5/2023/11/Aktiia_Bracelet_G1_User_Manual_v4.0_WEB_EN.pdf

Risk Management – Risk control

Example of risk controls

Medical device	*Hazard*	*Hazardous situation*	Inherently safe design	Protective measure	Information for *safety*
Syringe (for single use)	Biological contamination	Reuse after previous use on another patient	Self-destruction after use	Clear indication of first use	Warning against reuse
Implantable pacemaker	Loss of functionality	Pacemaker stops functioning due to early battery depletion	Reliable long-life batteries	Alarm before battery depletion	Information on typical battery lifetime
Mechanical patient ventilator	Air pressure	Software failure causes excessive pressure in patient airway	Blower incapable of delivering high pressure	Over-pressure valve in ventilator or in breathing hose	Instruction to use only breathing hose delivered by *manufacturer*
IVD blood analyser	Systematic error or bias	Incorrect result reported to clinician	Self-calibration	Metrologically traceable calibrators provided	Instruction to verify calibration with trueness controls
X-ray equipment	Ionising radiation	Staff exposed to stray radiation	Not feasible (stray radiation always occurs)	Lead shields and lead aprons	Information on radiation level in occupancy zones

ISO/TR 24971 Table 6

Risk Management – Risk analysis conclusion

Caution provided in the “about page” of the app

Always keep the indicated distance between the screen on which you are taking the test and your eyes. A different distance – shorter or longer – will impact your result thus making it imprecise. This test can be taken at 40 cm (reading vision) and 2 meters (distance vision).

You test one eye at a time. It is important that you cover the other eye as instructed during the test.

Information on residual risk provided in the IFU of the device

Important safety information, including residual risk and side effect, about Aktiia Bracelet / Important warning information:

	**This device may only be used for the purposes described in this User Manual. Aktiia cannot be held liable for damage or injury caused by incorrect use. Always follow the operating procedures described in this User Manual to measure your blood pressure accurately and safely.**
	**Aktiia Bracelet is designed as a device for personal use (single user) only. Do not share your device with others as it may result in inaccurate blood pressure readings.**
	**The strap of your Aktiia Bracelet contains silicone material. Avoid wearing the Bracelet in case of known allergy to silicone. Despite selecting medical grade materials for our device, skin irritation and skin reaction may occur as side effect. In case of skin irritation or reaction, stop wearing your Aktiia Bracelet to allow your skin to recover. Please also consult the section Care and maintenance of this manual. If symptoms persist or worsen, consult your doctor before using your Aktiia Bracelet.**

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Risk Management – Risk analysis conclusion

Risk status of the device – result of treatment plan

	Negligible (1)	Minor (2)	Moderate (3)	Major (4)	Catastrophic (5)
Improbable (1)	108	406 506 508	116 117 119 408 701	414 605	
Remote (2)		121 122 208 304 305 306 312 313 314 504 601 602 603 604 607	311 401 402 403 404 405 409 413 415 416 702	206 303 407 412 505 507	
Occasional (3)		111 112 113 114 201 202 211 214 215 302 410 411 510 704	205 207 209 210 212 213 216 217 218 219 310 502	203 204 302 501 503	
Probable (4)		106	307 308 309	109 110 115 509	
Frequent (5)			118		

Before mitigation

After mitigation

	Negligible (1)	Minor (2)	Moderate (3)	Major (4)	Catastrophic (5)
Improbable (1)	108 208	106 111 113 121 122 214 215 302 304 305 306 310 312 313 314 406 408 409 504 506 508 601 602 603 607 704	116 117 118 119 205 207 209 210 212 213 216 217 218 219 307 309 311 401 402 403 404 405 407 413 415 416 701 702	109 110 115 203 204 206 303 412 414 501 503 505 507 509 605	
Remote (2)		112 201 202 211 308 410 411 502 510 604			
Occasional (3)					
Probable (4)					
Frequent (5)					

The Risk Management Report typically contains the results of the risk management process in terms of how effective it was.

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Risk Management – Risk analysis conclusion

Residual risks

They are the risks that remain after risk control measures have been implemented. After applying all possible design improvements, protective measures, and alarms, these risk remain at a level which is significant.

Prior risk control

Cause / Failure Mode	Hazardous situation	Harm / Damage	S	P	RPN
The user is not positioned at 2m when performing the distance test	The user does not perform the test with the tested eyesight distance	The information provided to the user are inaccurate	3	4	12

Post risk control

Risk control / mitigation measure description	Evidence of Implementation	Additional risk?	S	P	RPN
User should acknowledge that the instructions are respected before proceeding to the test by ticking all checkboxes.	REQ-112, REQ-114, REQ-129	Yes uFMEA-11	3	3	9

The risk is still above the acceptable threshold

=> Residual risk to be communicated to the user

Risk Management – Risk analysis conclusion

Risk benefit assessment

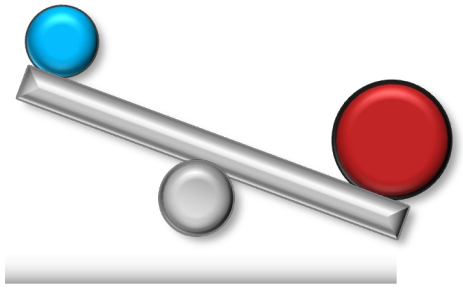
The risk-benefit assessment of a medical device shall demonstrate that its **intended clinical benefits**

- improved patient outcomes
- enhanced safety,
- increased quality of life

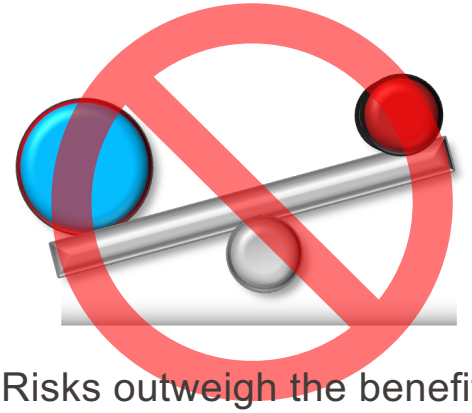
outweigh the potential risks, including

- device malfunctions,
- user errors,
- adverse effects,

while ensuring that **all identified risks are mitigated** through robust design, regulatory compliance, and appropriate risk management strategies.



Benefits outweigh the risks

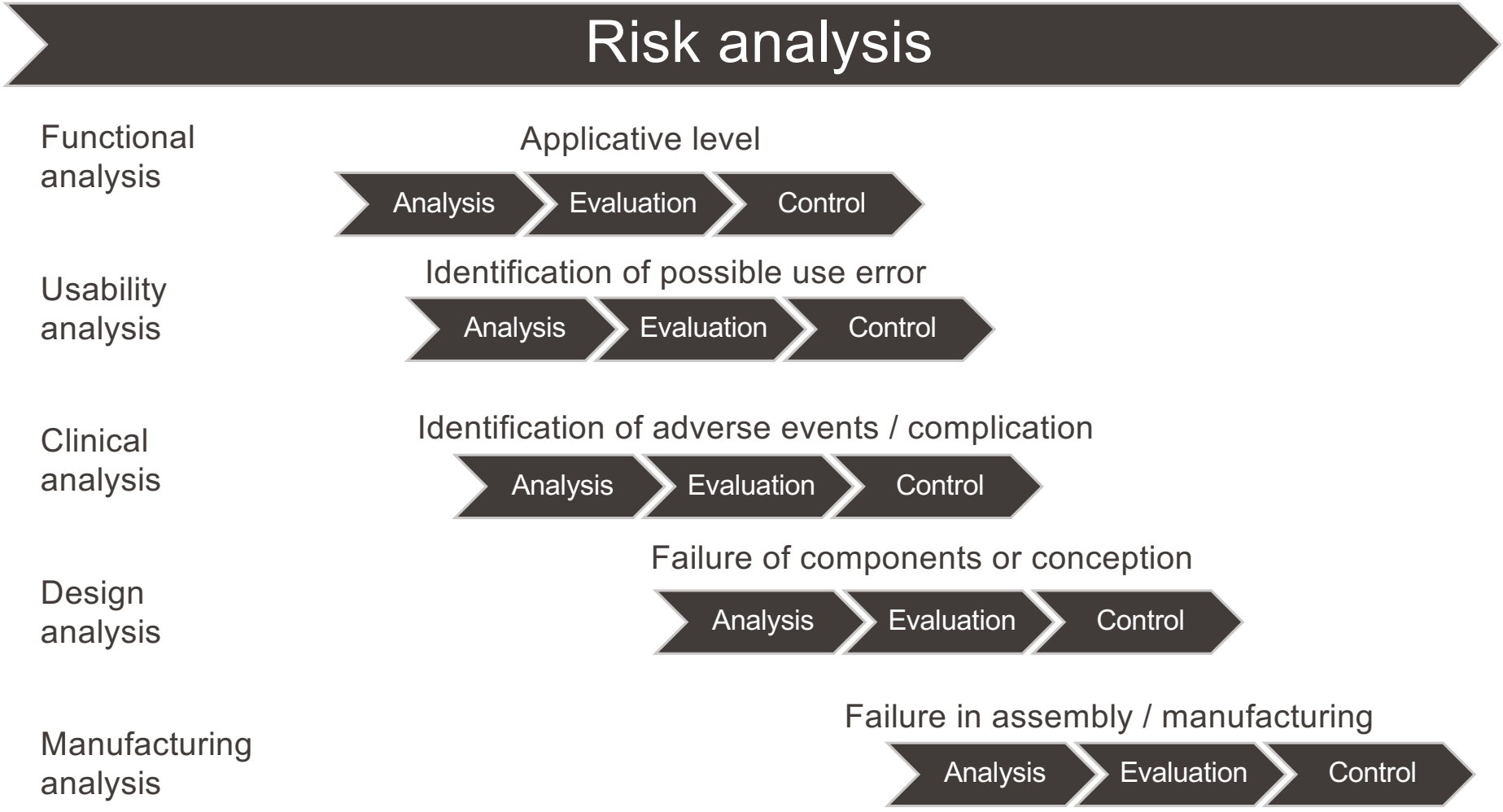


Risks outweigh the benefits

Benefits for patient

Residual risk of device or risk of procedure

Risk Management – Scope

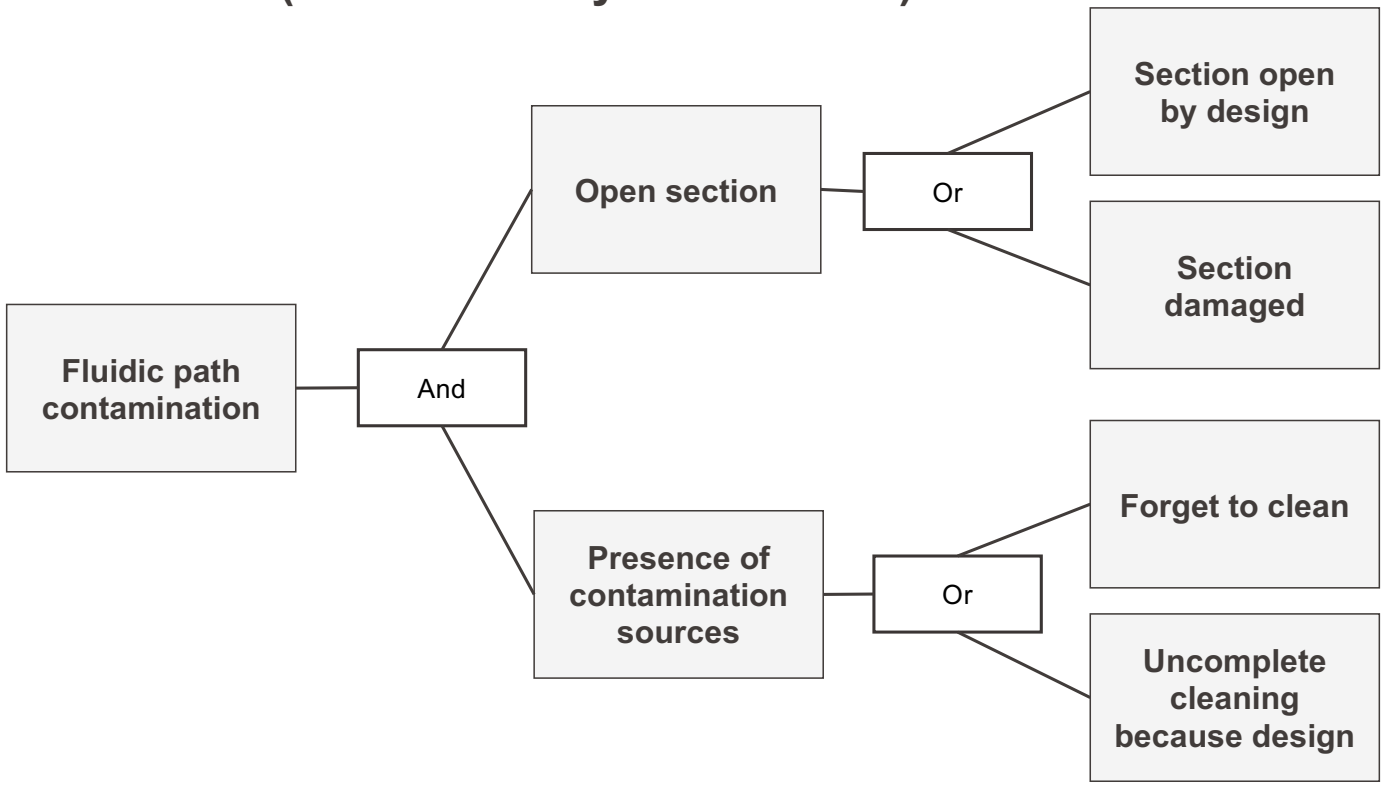


Risk Management – Methodologies

- **Preliminary Hazard Analysis** (PHA) is a technique that can be used early in the development *process* to identify the *hazards*, *hazardous situations*, and events that can cause *harm* when few of the details of the *medical device* design are known
- Fault Tree Analysis (FTA) and Event Tree Analysis (ETA) are especially useful in *safety* engineering, early in the development *process*, for the identification and prioritization of *hazards* and *hazardous situations* and possible *risk control* measures as well as for analysing the consequences of adverse events
- **Failure Mode and Effects Analysis** (FMEA) is a technique by which effects or consequences of individual components are systematically identified and is more appropriate as the design matures and the failure modes are better understood
- Hazard and Operability Study (HAZOP) is typically used in the early stages of the development *process* to study deviations from the intended performance
- Hazard Analysis and Critical Control Point (HACCP) is typically used in the later stages of the development *process* to verify and then optimize design concepts or changes

Risk Management – Methodologies

An example of a medical device that can experience fluidic path contamination (i.e. hemodialysis machine).



A hemodialysis machine is a device that cleans a patient's blood by filtering out waste, toxins, and excess fluids when the kidneys cannot do so.

Risk Management – Risk management lifecycle

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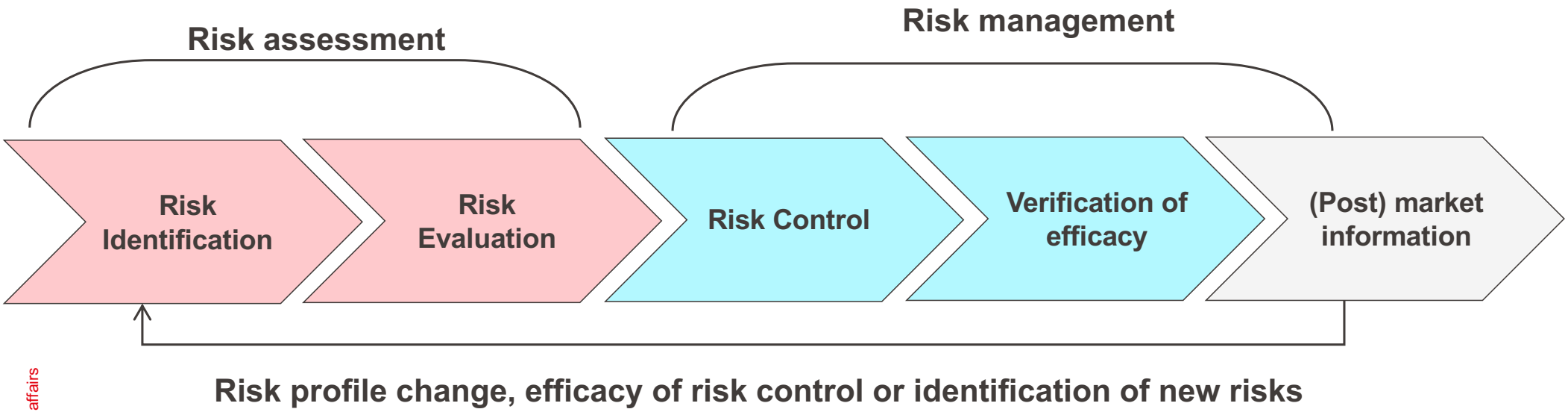
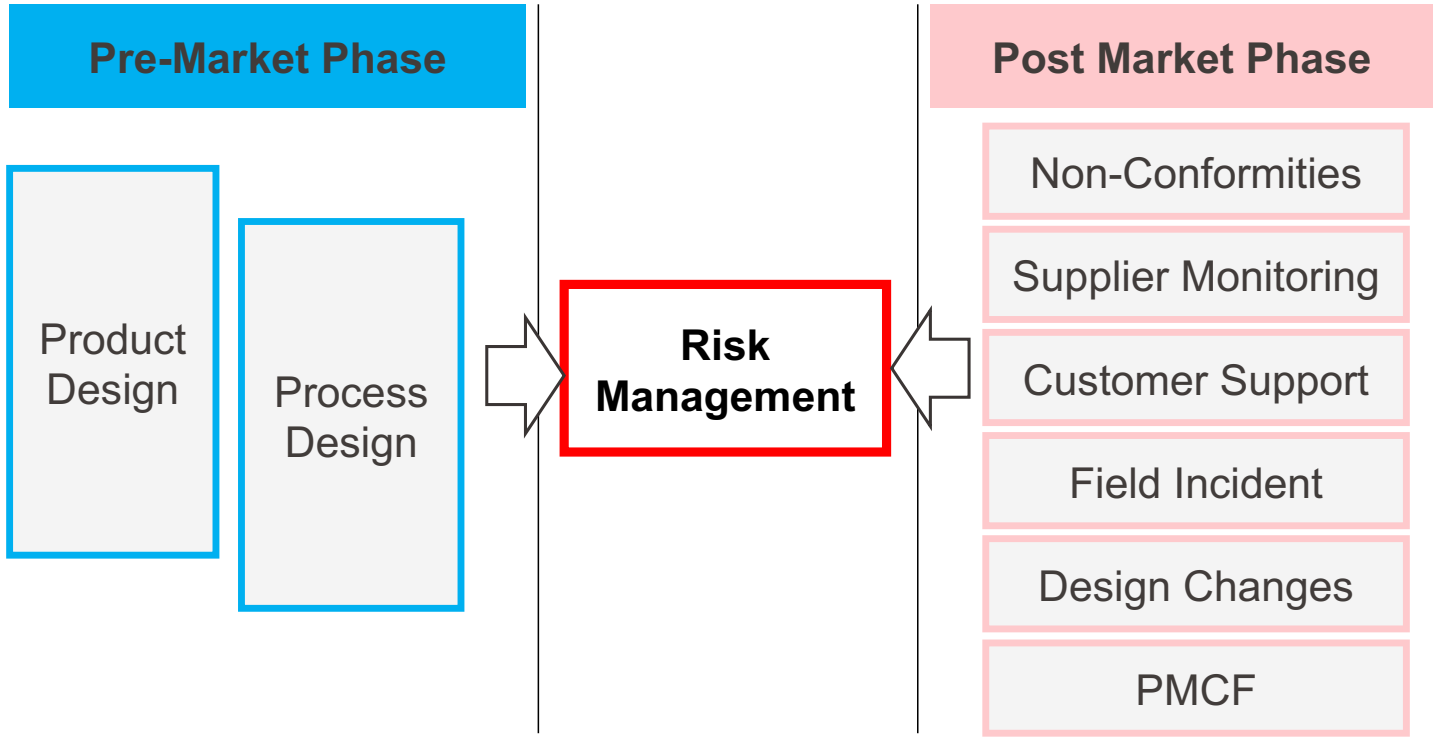
Risk evaluation cycle



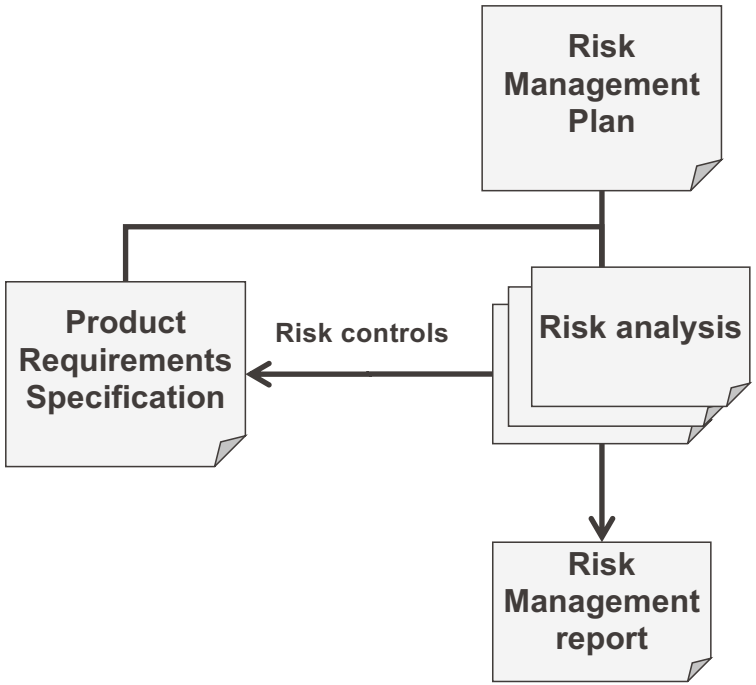
Risk Management – Risk management lifecycle

Risk evaluation activities



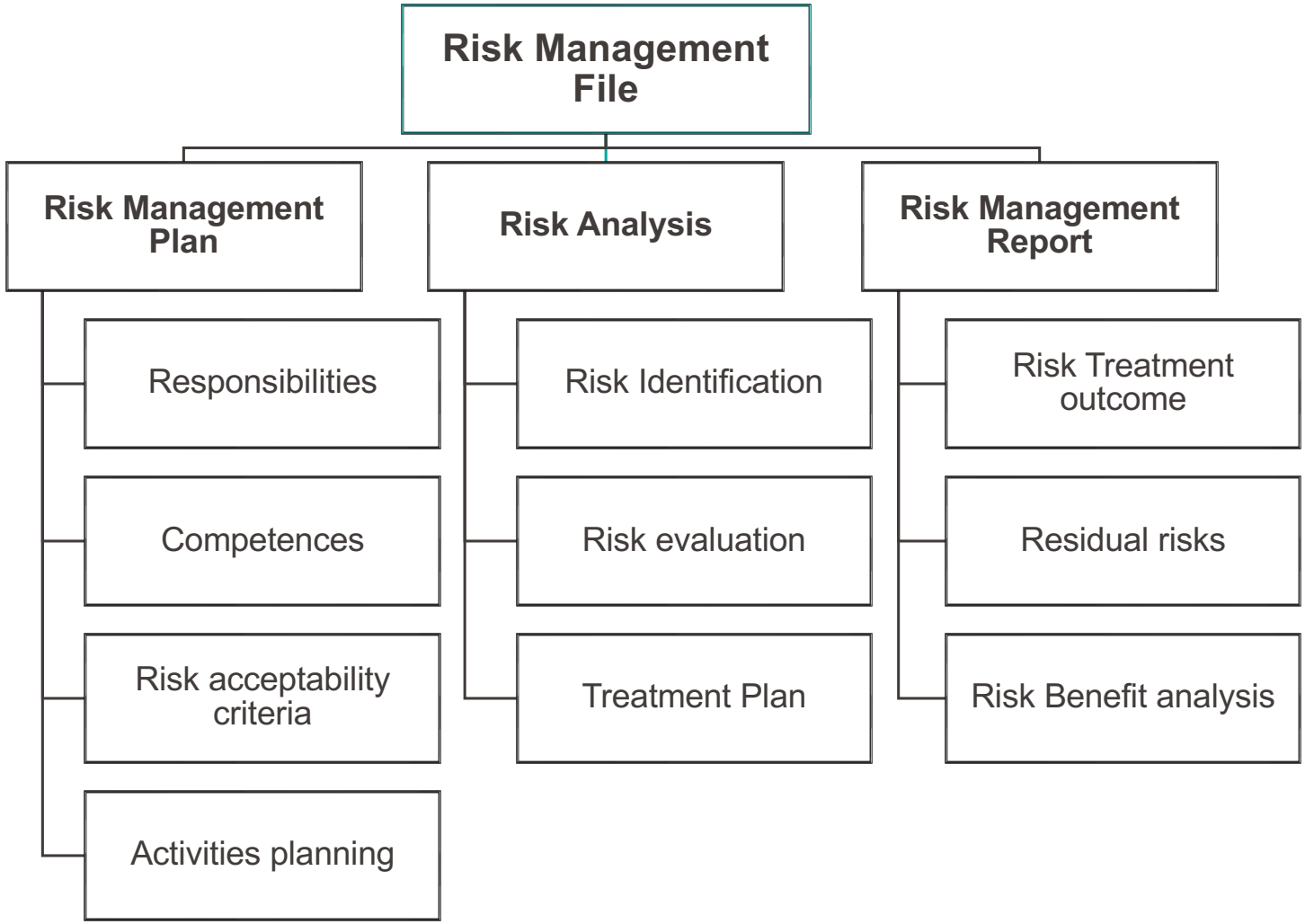
Risk Management – Risk management documentation

Key elements of the risk management file



- The risk management activities shall be planed at the beginning of the development process.
- The risk analyses are performed during the product lifecycle.
- Codification of risk is recommended as link between risk analysis and requirements (mandatory for software i.e. for reference to mitigation measure).
- A link between risk management and change management is to be integrated in the development process.
- The risk management outcome shall be formalized in a report

Risk Management – Risk management documentation



Risk Management – Risk management documentation

Identification of required competences

	Project Manager	Hardware expert	Software expert	Clinical expert	Manufacturing	Quality Assurance & Regulatory
Phase I	R	-	-	A	-	A
Phase II	R	R	R	R	-	-
Phase III	R	R	R	A	A	-
Phase IV	R	R	R	A	A	R
Phase V	R	R	R	A	A	R

R – stands for required qualification, A – stands for if appropriate

Q&A


WALLY, I DISCOVERED A DEADLY SAFETY FLAW IN OUR PRODUCT. WHO SHOULD I INFORM?
www.dilbert.com scottadams@aol.com
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BUT MY NEGLIGENCE COULD CAUSE THE DEATHS OF A DOZEN CUSTOMERS.
THE FIRST DOZEN IS ALWAYS THE HARDEST.