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Risk based approach in Lyophilizer projects and validation

Focus

Risk based approach as a design tool

- to define and to verify the “real” process equipment requirements
- to define project responsibilities (e.g. with supplier) and
- to define the limitations to avoid over sizing, over validation and “dead paper”

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Content

- Overview of risk management tools
 - Basic overview of tools which might be used for quality risk management
 - Evaluation of risks and possibilities of risk reduction
- Risk management as part of project management
 - Project focus on “real” process requirements
 - Opportunities
 - to improve hand shakes between customer and suppliers
 - to increase transparency and communication within projects
 - to optimize personnel placement due to quality focus
 - to avoid “dead paper” within validation and documentation

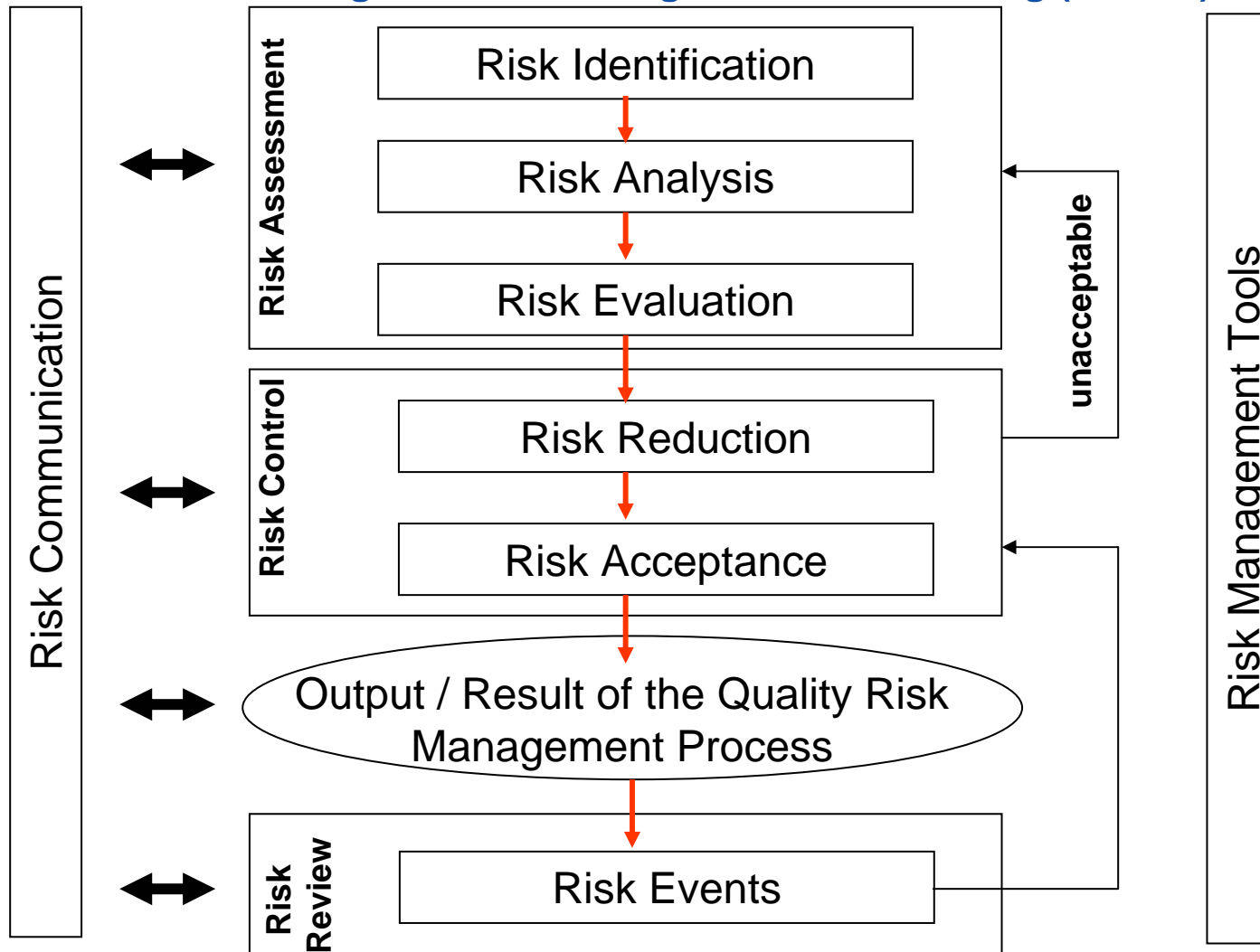
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Overview of risk management tools- ICH Q9

- Quality Risk Management according to ICH Q9:
 - “The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and
 - The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.”

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Overview of risk management tools- Organisation according (ICH Q9)



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Overview of risk management tools- ICH Q9 Definitions

- Risk Assessment
 - consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.
 - 1. What might go wrong?
 - 2. What is the likelihood (probability) it will go wrong?
 - 3. What are the consequences (severity)?
- Risk identification
 - is a systematic use of information to identify hazards referring to the risk question or problem description.
- Risk analysis
 - is the estimation of the risk associated with the identified hazards.
- Risk evaluation
 - compares the identified and analyzed risk against given risk criteria. Risk evaluations consider the strength of evidence for all three of the fundamental questions.

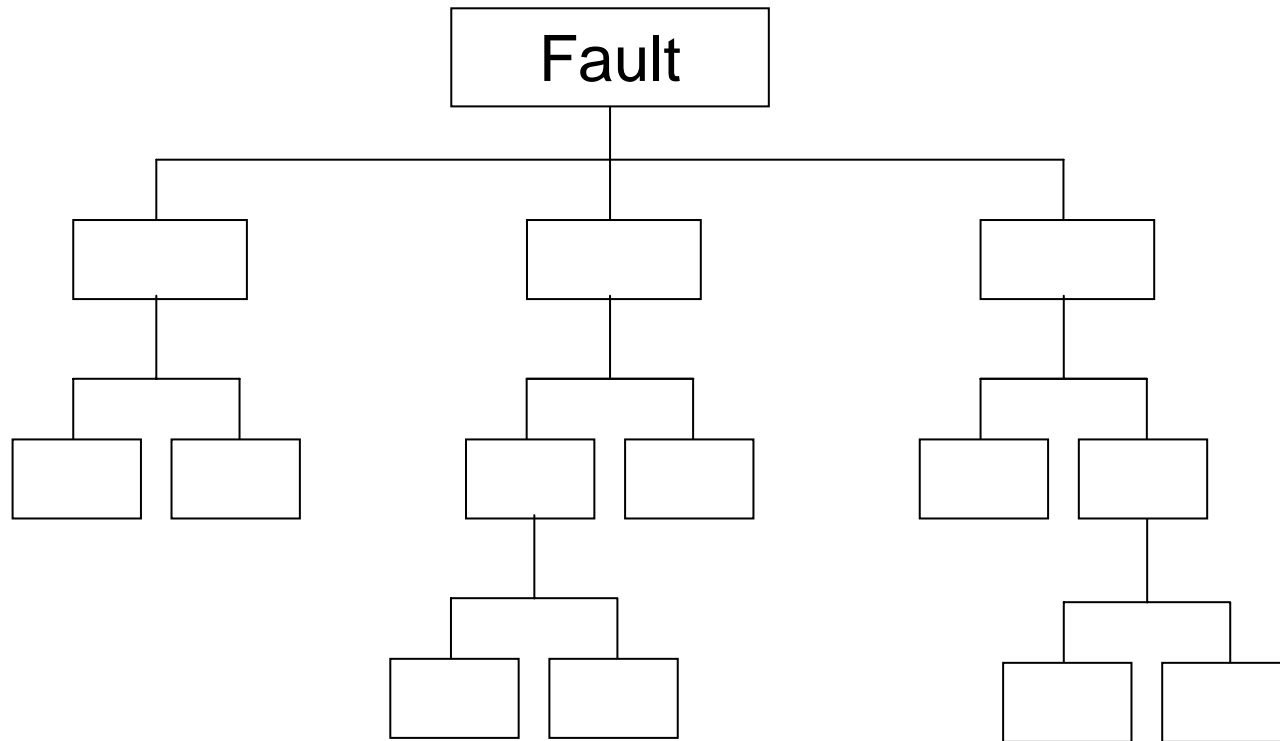
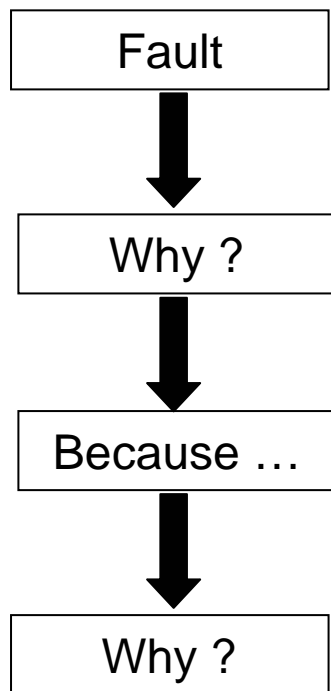
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Overview of risk management tools- ICH Q9 Definitions

- Risk control
 - might focus on the following questions:
 - Is the risk above an acceptable level?
 - What can be done to reduce or eliminate risks?
 - What is the appropriate balance among benefits, risks and resources?
 - Are new risks introduced as a result of the identified risks being controlled?
- Risk reduction
 - focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level.
- Risk acceptance
 - formal decision to accept the residual risk.
- Risk communication
 - is the sharing of information about risk and risk management between the decision makers and others.
- Risk review
 - The output/results of the risk management process should be reviewed to take into account new knowledge and experience.

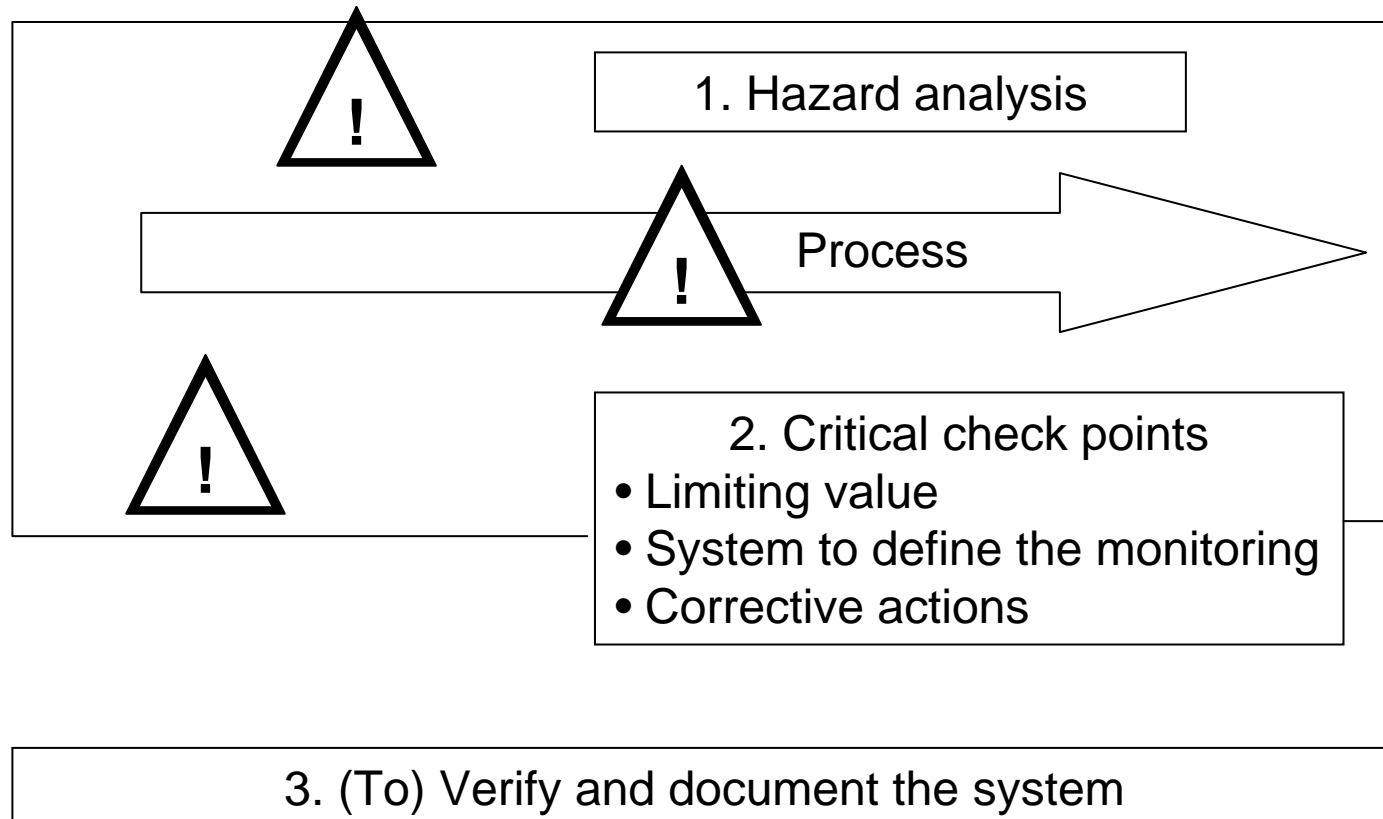
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Overview of risk management tools- Methods: Fault Tree Analysis, FTA



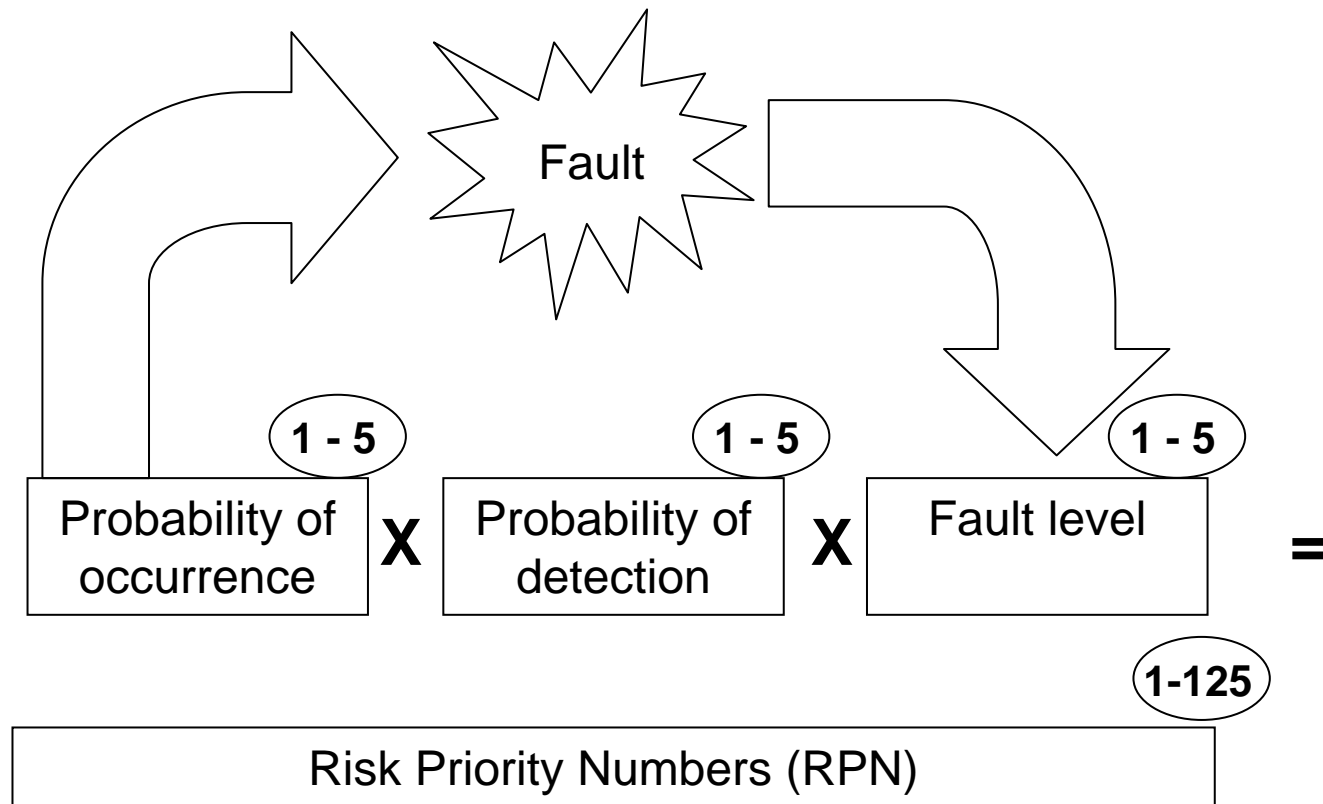
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Overview of risk management tools- Methods: HACCP-Method



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Overview of risk management tools- Methods: FMEA(Failure Mode Effect Analysis)

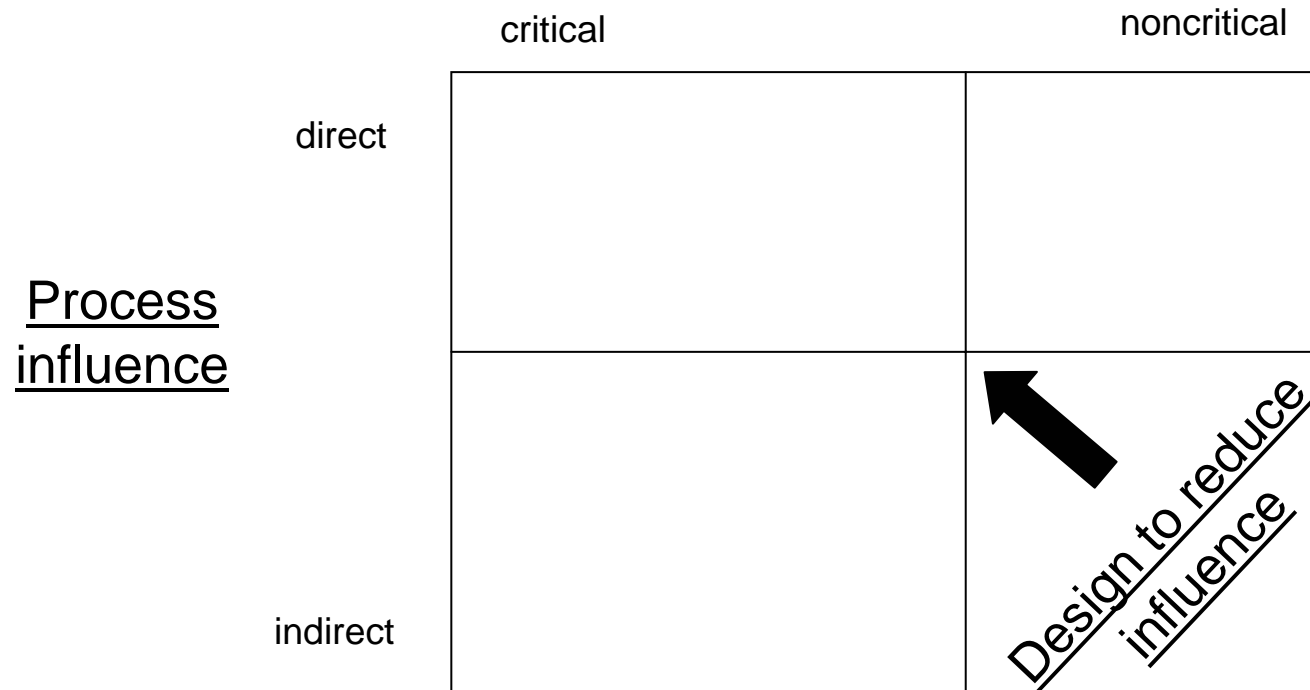


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Risk management as part of project management- Design Phase

Technical Design

Components

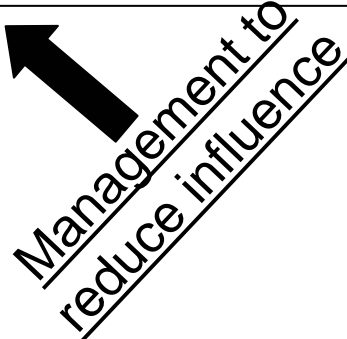


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Risk management as part of project management- Design Phase

Project Handling

Influence of involved people
(e.g. User, Engineering, Supplier, QA, PM.....)

	critical	noncritical
direct		
<u>Chosen system/ techniques</u>		
indirect		

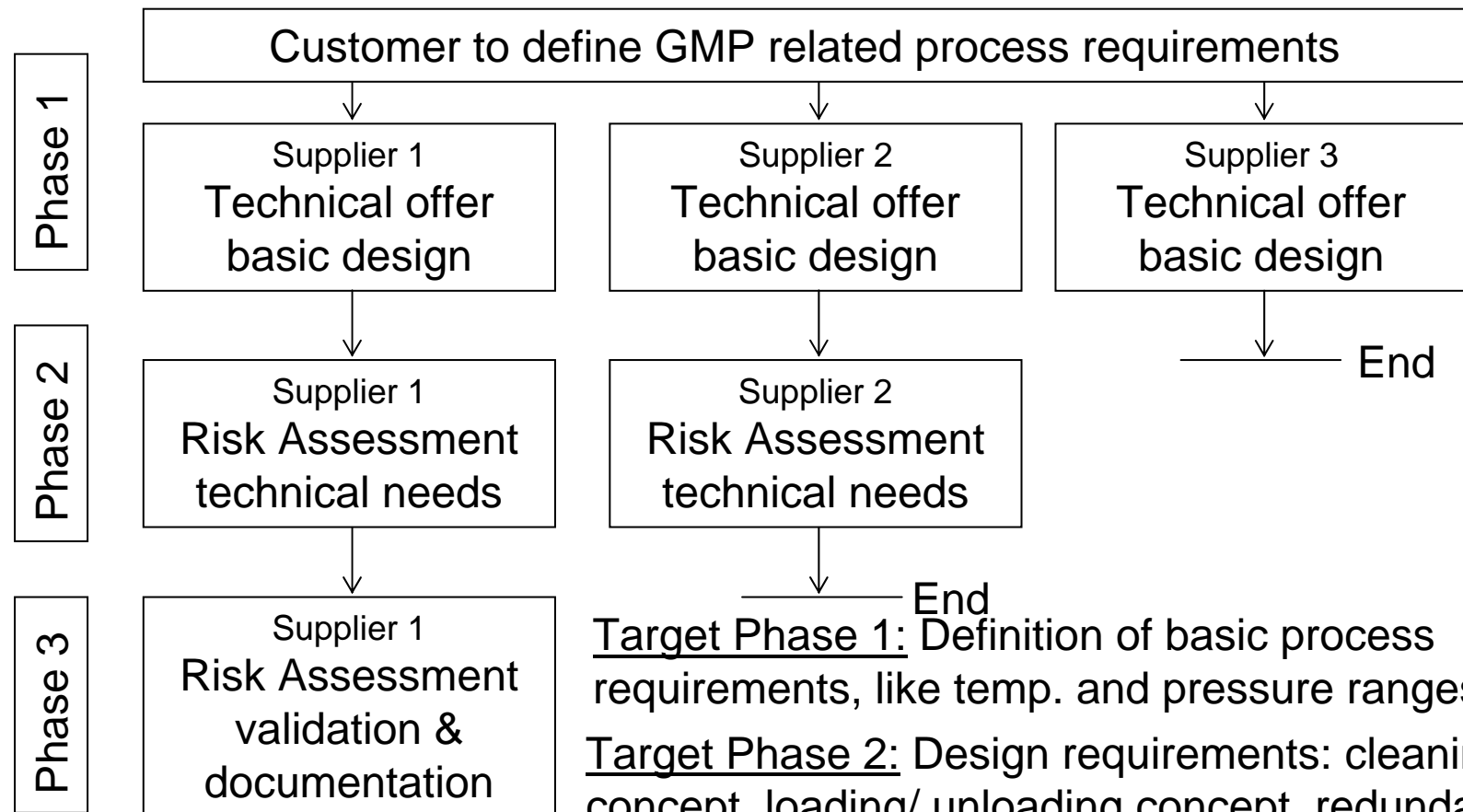
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Risk management as part of project management- Design Phase

- The highest risk is not to get what is required
- Key questions for each phase:
 - What are the real required features?
 - Where starts the “nice to have” area?
 - Who should do the activity?

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Risk management as part of project management- Design Phase



Target Phase 1: Definition of basic process requirements, like temp. and pressure ranges

Target Phase 2: Design requirements: cleaning concept, loading/ unloading concept, redundancy

Target Phase 3: Definition of Project Control, Responsibilities, Test and Documentation, Summary

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Risk assessment should be an initial part of each project phase because:

- Design and functionality is based on current requirements
- GMP and safety related components will be detected
- Critical process parameters, steps and events will be determined
- Project team members will get a deeper view into the process
- Interdisciplinary teams ease further communication within the project (e.g. engineering vs production vs QA)

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Risk assessment should be an initial part of each project phase because:

- Priorities for the qualification and validation activities will be identified
- Documented evidence and description of the scope of qualification and validation activities will be clarified
- Traceability is assured from risk detection to end of validation
- Testing and documentation can be limited to previously defined objects. No 'dead paper'!

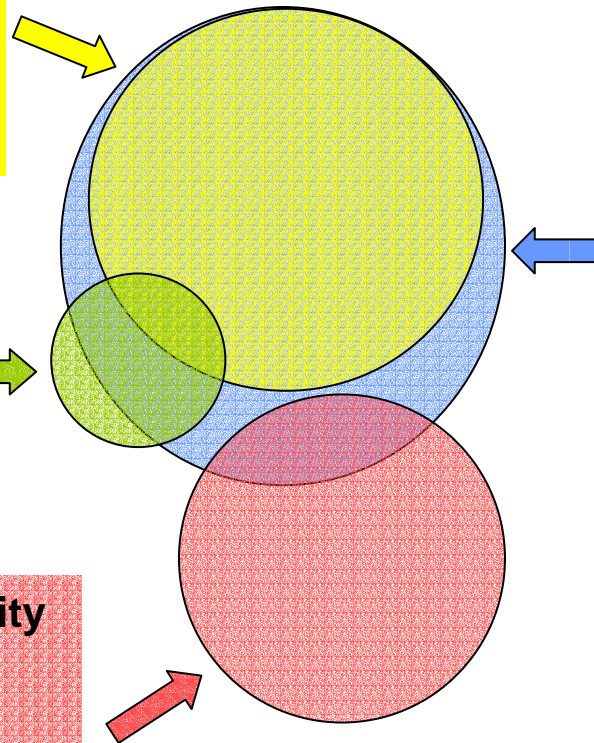
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Example for phase 3: Supplier part in qualification activities

Supplier enhanced quality activities, i.e.
- qualification tests (IQ and OQ)

Services i.e.
Calibration,
maintenance

Supplier standard quality activities, i.e.
- **Commissioning** tests (adjustments, leak tests, in house calibration, change management, performance tests....)
- **FAT and/ or SAT**



Customer activities, i.e.:
- Validation Master Plan (VMP)
- Operating Procedures (SOPs)
- Qualification of personnel (training and employment)
- Calibration and Maintenance
- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Performance Qualification (PQ)
-

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Example for phase 3: Supplier part in qualification activities

Supplier generates qualification documents and performs testing

Advantage

- Deep knowledge of the system
- Deep knowledge of validation of the equipment with different customers
- Combination between commissioning and qualification activities can reduce lead time
- Just in time correction of findings possible (under change control)

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Example for phase 3: Supplier part in qualification activities

Supplier generates qualification documents and performs testing

Disadvantage

- Possibly additional GMP or customer standard training required
- Customer has to understand the approach and has to implement supplier standard into internal standard
- Not all tests can be performed by supplier (e.g. SOPs, interfaces to other equipment)

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Example for phase 3: Supplier part in qualification activities

Customer generates qualification documents and performs testing

Advantage

- Documents in accordance to internal standard
- Experience with inspections by authorities (e.g. FDA)
- Qualification activities are a good (user) equipment training

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Example for phase 3: Supplier part in qualification activities

Customer generates qualification documents and performs testing

Disadvantage

- Limited capacities
- Tests partly only with supplier performable
- Generation of test procedures takes a long time due to limited equipment experience

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Disadvantages of risk based project design

- Difficult to estimate the cost of the project
- Difficult to estimate the duration of the project
- Time and personnel intensive start phase
- Open discussion may lead to uncomfortable results (e.g. chosen supplier is not sufficient)

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Advantages of risk based project design

- Lyophilizer will fulfil the requirements
- Higher liability due to technical limitation to “real” needs
- At the end of common design phase the documentation and validation amount is clearly defined

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Conclusion

- Clarifications in early project phases (e.g. scope, terms and ,way of doing‘) save time, money and reduce confrontations at the end
- Common understanding supports confidence for both partners
- Active participation during the entire project guarantees the fulfilment of expectations
- Supplier knowledge should be used where ever reasonable

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Conclusion

- Commissioning and Qualification is partly as well optimization of the equipment and training of employees
- Documentation and testing is part of the project and not an 'add on'
- Amount of documentation and testing should be limited to the real needs. No 'dead papers'!
- Design is based on requirements not on standard specifications. No 'dead functionality'!

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Questions ?

