Management of product transfer projects

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Content

1. Technology Transfer Project Structure
2. Risk management
2. Best practices
3. Workshop “Create transfer project plan”

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PROJECT STRUCTURE

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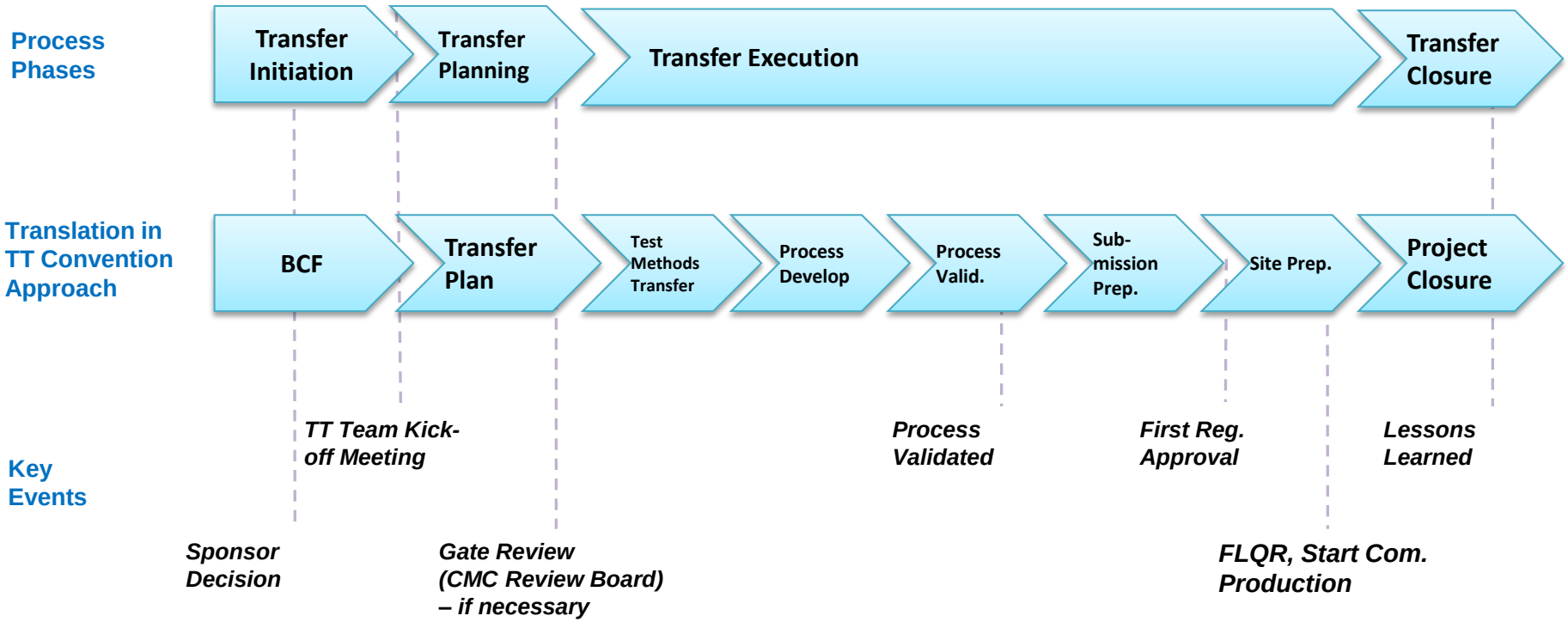
Technology Transfer Process: Phases



A planned systematic sequence of activities that is followed in order to transfer manufacturing of a pharmaceutical product from one unit to another

Phase 1: Transfer Initiation- BC

Transfer Initiation

Objective

Preparation of a TT business case to gain funding and approval for the project

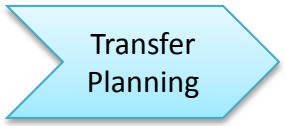
- **Before beginning** this phase, you will need:
  1. Clear understanding of the idea and business need with assumptions
  2. Overview of the current situation and the proposed situation

- **At the conclusion** of this phase, you will have produced:
  1. Project initiation decision
  2. If approved, funding for the entire project

Key Activities

1. Create high-level process/ testing/ quality & regulatory requirement
2. Conduct high-level gap assessment
3. Gather cost estimates
4. Provide Business Case for Decision

Phase 2: Transfer Planning



Objective

- The aim of this phase is to ***evaluate the risks associated with the transfer,*** establish a suitable risk control strategy and define the deliverables of the project.

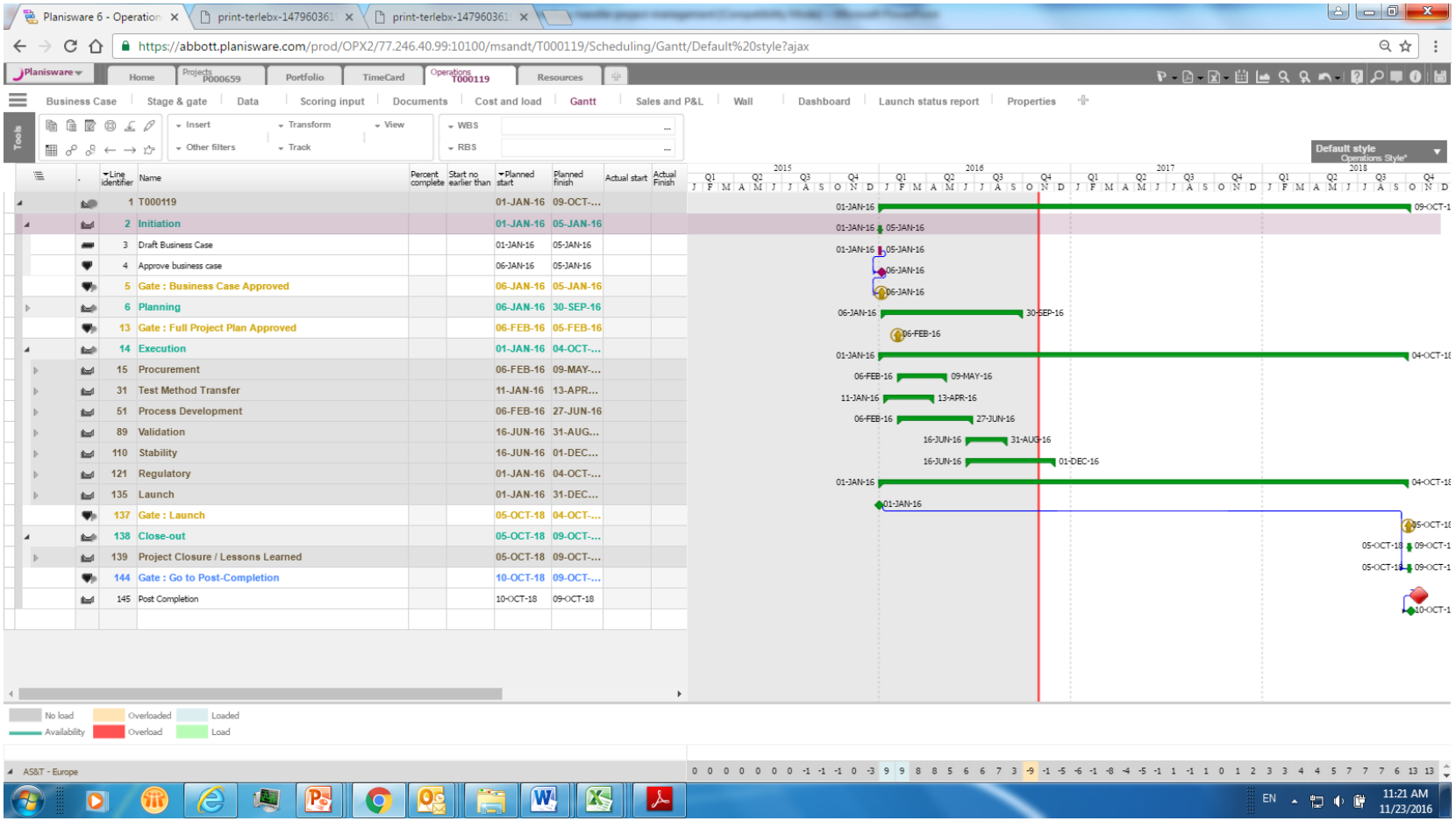
- **Before beginning** this phase, you will need:
  1. Approved business case

- **At the conclusion** of this phase, you will have produced:
  1. Approved TT Plan
  2. Agreement on deviations from approved business case
  3. Passed Gate Review (if necessary)

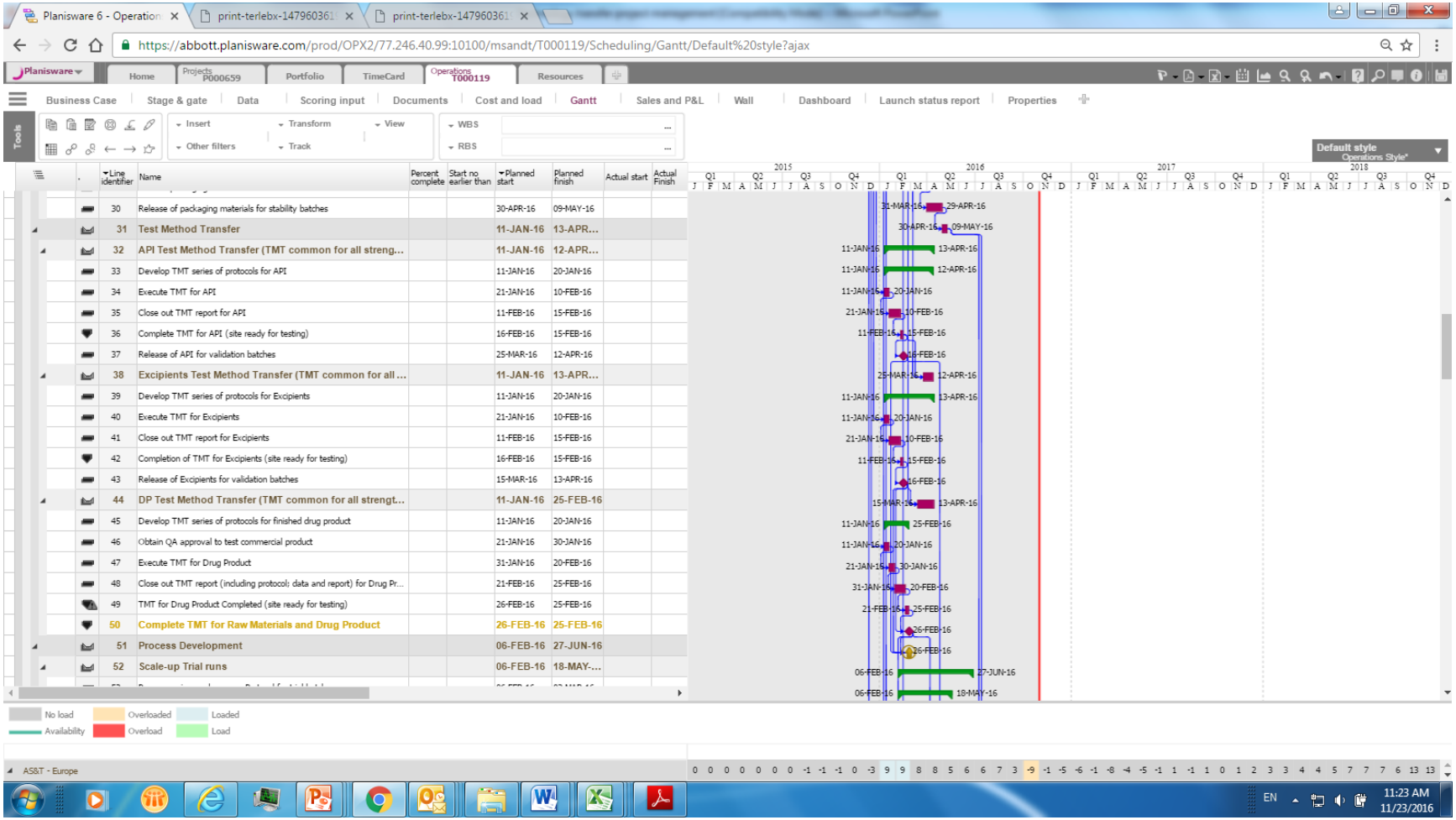
Key Activities

1. Form project team and structure
2. Gather current product and process data
3. Conduct risk assessments and define risk control strategies
4. Define the test method transfer, process transfer and validation approach
5. Define Regulatory Strategy
6. Define required activities for launch and commercial production
7. Validate business case cost and time assumptions
8. Finalize Transfer Plan and deliverables
9. Organize Gate Review (if necessary)

Project Gantt Chart (high level), example



Project Gantt Chart (high level), TMT example



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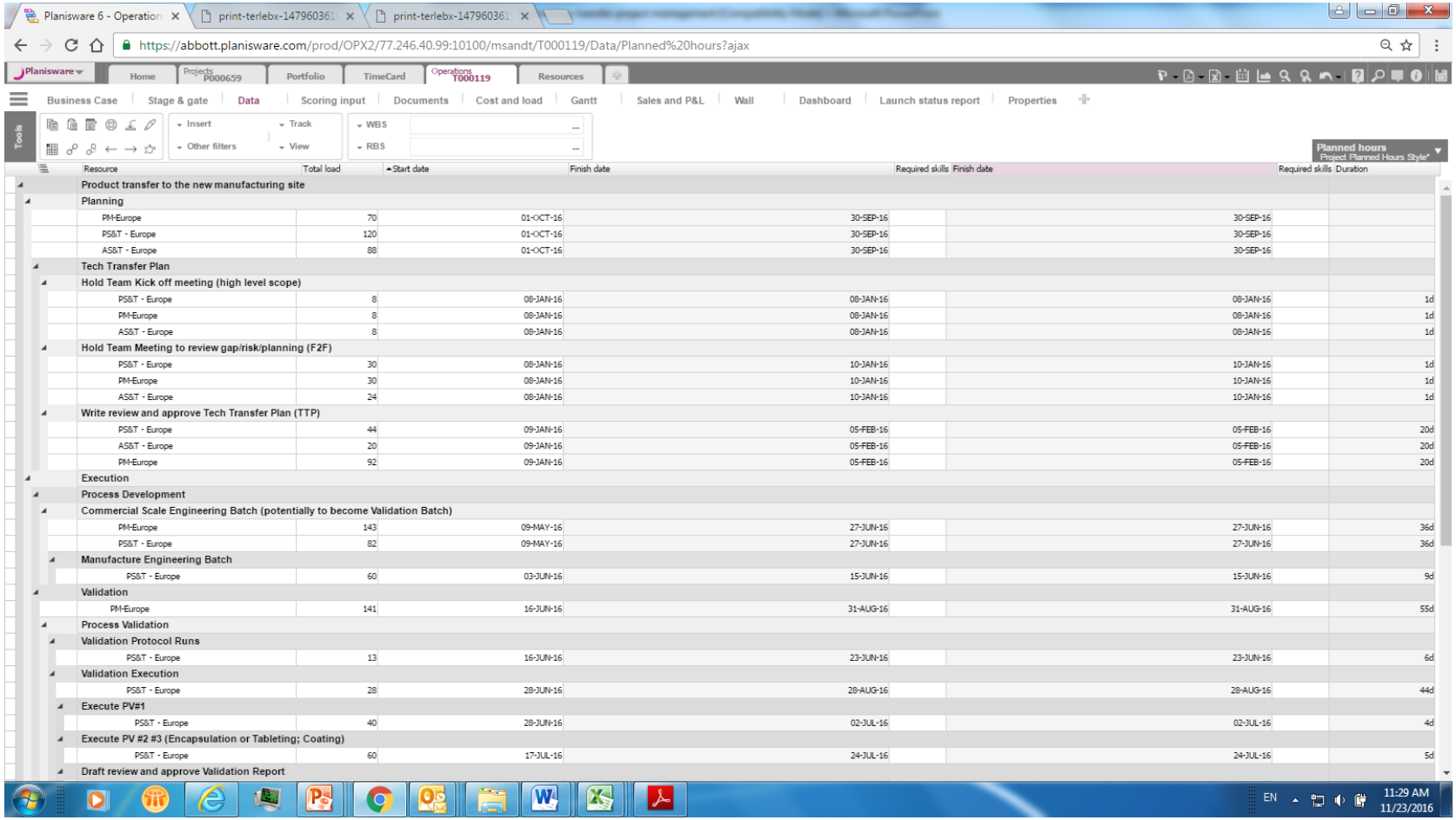
Internal resource planning, example



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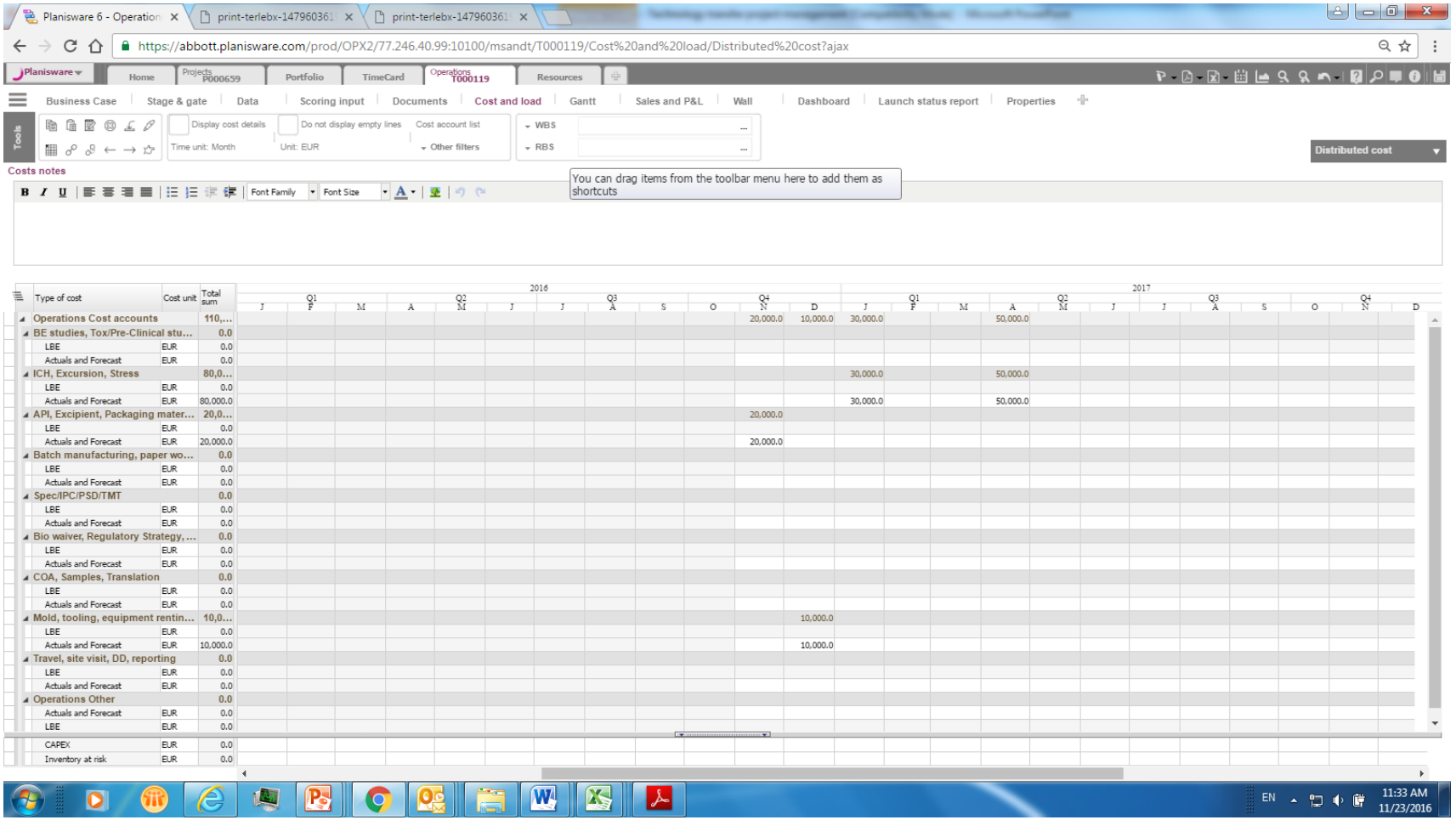
External resource planning, example



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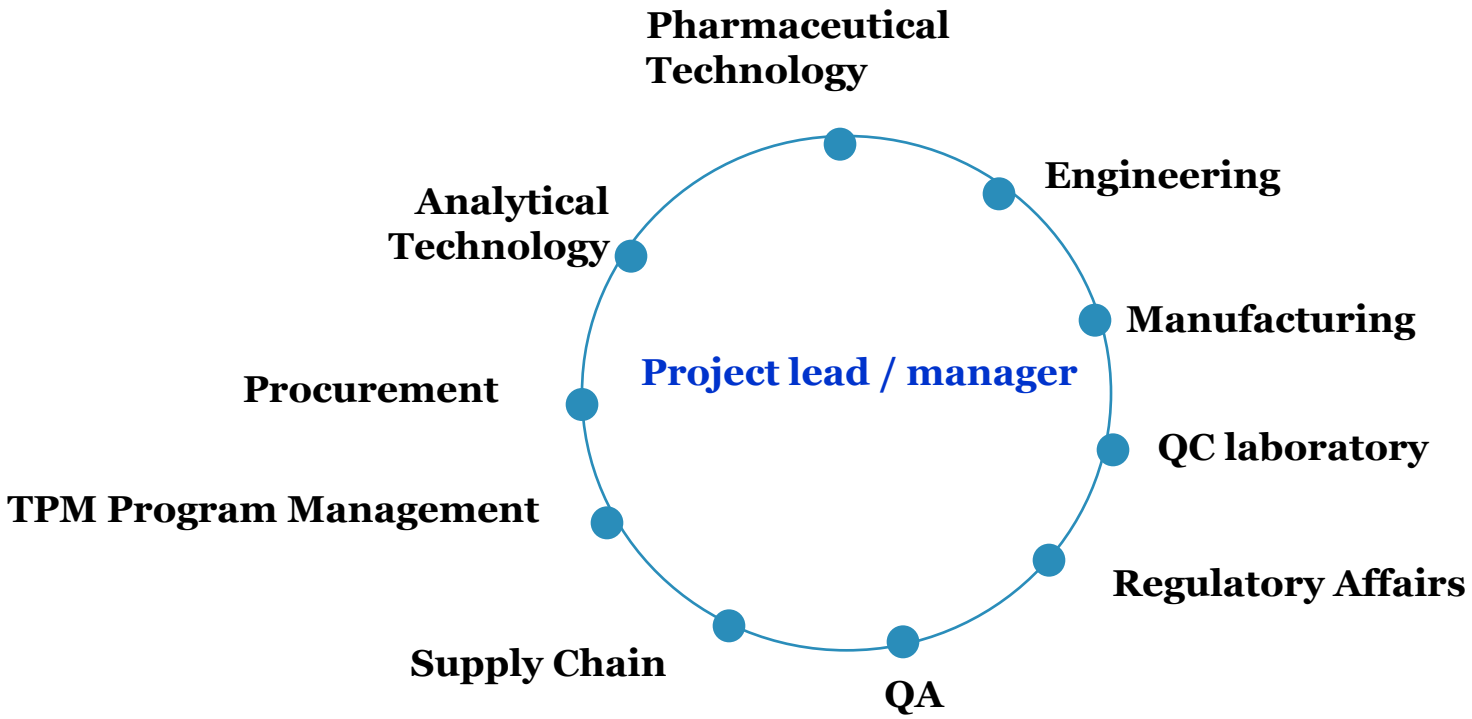
Project team (work stream)



Ad-hoc: Marketing, Market access, Finance.

Project Transfer Plan: typical information

- **Project overview**
  - Scope - Executive Summary
  - Supply Chain Flows
  - High level Transfer Strategy

– **Project Team**
  - Team members - RACI Matrix
  - Communication and meeting frequency
  - Issue elevation process and gate reviews

– **Technology transfer technical elements and proposed change management strategies:**
  - Composition – unit formula - Raw materials - Function of components and source – Change strategy
  - Batch sizes - Manufacturing formulas Sending Unit - Receiving - Changes strategy
  - Manufacturing Process and Manufacturing Instructions, including In Process Controls (from CTD) - Sending Unit - Receiving Unit - Changes strategy
  - Packaging requirements – Packaging formula – Packaging materials- specifications
  - Product characteristics necessary for cleaning validation - Cleaning efficiency assessment / validation approach

– **Technology transfer technical elements and proposed change management strategies cont'd:**
  - EHS considerations - Material safety data sheet - EHS analysis and mitigation approach
  - Analytical Methods and controls
    – Specifications
    – Test Methods
    – Test Methods transfer strategy, including risks and mitigation strategy
  - Manufacturing Risk Assessment - mitigation strategy

– **Process validation** (including supportive process development activities, if necessary) and Stability assessment strategy, with reference to quality and regulatory needs

– **Regulatory Strategy**
  - Source documents reference and documentation update strategy

– **Appendix 1**: EHS API, Drug Product & Packaging Transfer Checklist

– **Appendix 2**: High level Transfer Schedule

Phase 3: Transfer Execution

Transfer Execution

Objective

- **To execute the deliverables as defined in the TT plan and gain market approval**

- **Before beginning** this phase, you will need:
  1. Approved TT plan
  2. Passed Gate Review (if necessary)
  3. Agreement on deviations from approved business case

- **At the conclusion** of this phase, you will have produced:
  1. Complete hand-over of robust process and/ or analytical method to receiving unit
  2. Market approval
  3. FLQR approval
  4. Launch readiness
  5. Passed Gate Review (if necessary)

Key Activities

1. Ensure QA audit is in place
2. Complete receiving unit site readiness and finalize receiving site quality documentation
3. Complete Test Method Transfer
4. Perform engineering/ registration/ validation/ batches/ EHS monitoring (as required)
5. Initiate stability and hold time studies
6. Prepare dossier for regulatory submission
7. Submit dossier and respond to deficiency questions
8. Complete FLQR approval
9. Define post-validation monitoring plan (if applicable)
10. Prepare the site for commercial production (launch readiness)
11. Organize Gate Review (if necessary)

Phase 4: Transfer Closure

Objective

- To complete the TT process
- To capture lessons learned in order to facilitate improvements
- To complete hand-over to commercial production phase

- **Before beginning** this phase, you will need:
  1. Completed the hand-over of robust process and/ or analytical method to receiving unit
  2. Gained Market approval
  3. Gained FLQR approval
  4. Completed launch readiness
  5. Passed Gate Review (if necessary)

- **At the conclusion** of this phase, you will have :
  1. Disbanded TT project team
  2. Increased team member TT skills and abilities
  3. Completed lessons learned
  4. Delivered the value to the business as defined in the business case
  5. Confirmed that all non-quality documents are captured in approved repository

Key Activities

1. Perform lessons learned session with project TT team (and as appropriate with sending and receiving units)
2. Conduct closure meeting to
   - Ensure that business case is achieved
   - Confirm that all required steps outlined in TT plan have been completed
   - Transfer ownership and documentation to appropriate function
3. Implement post-validation monitoring (if needed)
4. Celebrate successes

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RISK MANAGEMENT

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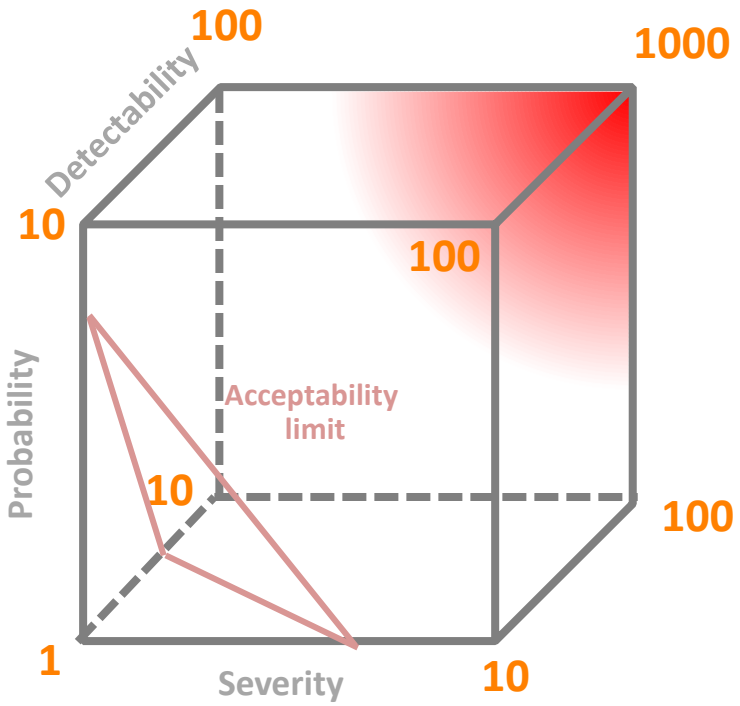
FMEA (ich q9)

- The **Failure Mode Effect Analysis** responds to the need of anticipating and possibly moderating/avoiding unexpected/undesired/critical situations a process/product/system may incur.

- Simply put, the **basic FMEA** is a structured approach to:
  - **Identifying the ways in which a product/process/system can fail**
  - **estimating risk associated with the failure**
  - **identifying and prioritizing the actions that should be taken to reduce risk**

Risk evaluation

- Risk related to Failure Mode is evaluated:
  - for each Failure Mode
  - for the overall system/process/product in scope
- Risk level may be:
  - **accepted** (nothing is done)
  - **eliminated or reduced** to acceptable level through **prevention/moderation actions**
- Risk acceptance criteria are set according to regulatory constraints/and/or business objectives,



Risk Priority Number calculation

The **Risk Priority Number** (RPN) is an index used to **evaluate failure risk** and identify critical areas eligible/priority for corrective/preventive action

Risk = Event probability x Event consequences (damage)

RPN = P x D x S

Item RPN range
(1-1000)

Failure occurrence probability
(score 1-10)

Detection probability
(score 1-10)

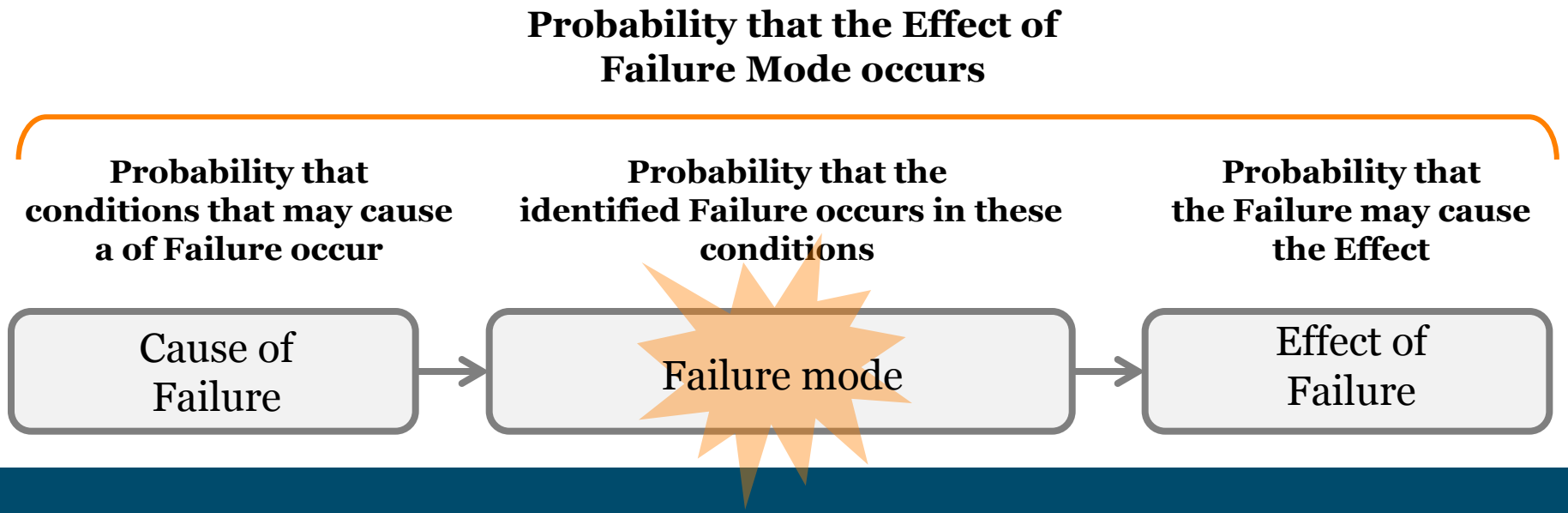
Impact severity (damage)
(score 1-10)

Probability that the whole causal chain cause-failure-effect may occur

Undetected failure impact may continue in time/propagate across the system

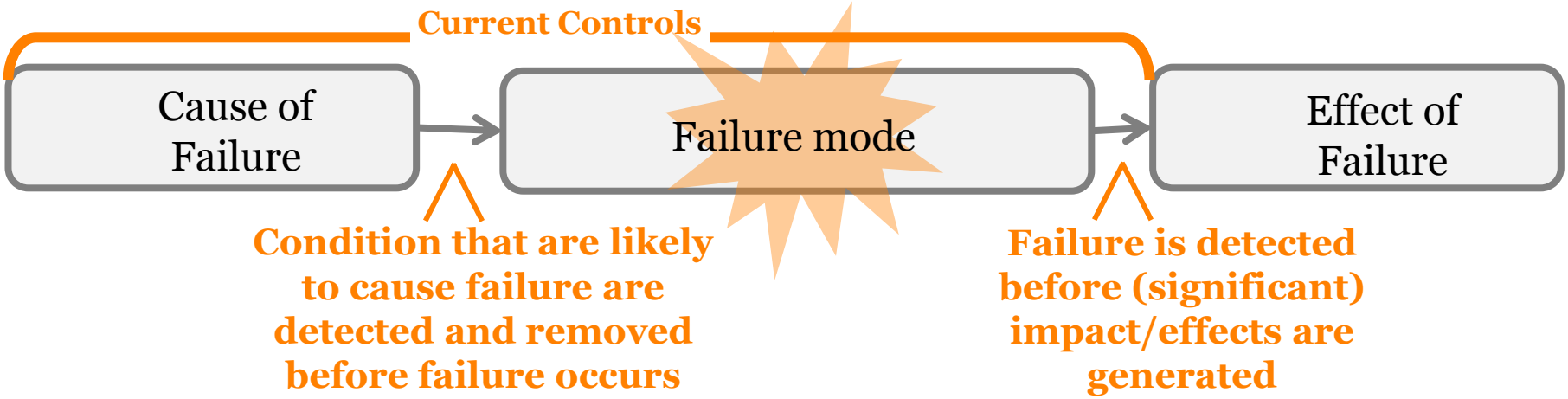
Probability

- **Estimates the probability that the entire sequence Cause/Failure/Effect may occur.**
- Probability estimation may involve:
  - quantitative evaluation of historic occurrences
  - **qualitative evaluation according to subjective experience, expertise**



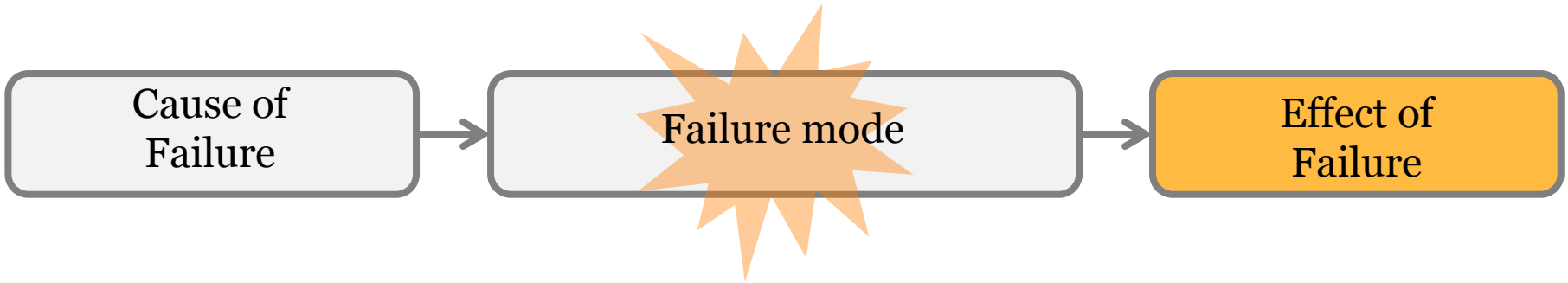
Detectability D

- **Estimates the likelihood** (or in negative terms the difficulty) **of identifying and preventing/interrupting the sequence cause-failure-effect**
- Failure impact may extend in time (impact continues until failure is resolved) or may spread across process/system/product (failure triggers other failures). Effect of failure may be strongly dependent on mechanism/timing of failure detection.
- A failure may have more than one/many Causes.



Severity S

- **Estimates the impact/damage caused by the Failure**
- Depending on the scope/domain of analysis:
  - may involve different actors (customer, user, process owner, operator)
  - may and multiple a wide range of impacts/damages, from annoyance, to efficiency reduction (waste) to personal death/injury to operator/customer/owner
- A Failure may have more than one/many effects;



FMEA deliverable

Process/Product
Failure Modes and Effects Analysis Form
(FMEA)

Processor Product Name:		Prepared by:	Page ___ of ___
Responsible:		FMEA Date (Orig) _____ (Rev) _____	

Process Step / Input	Potential Failure Mode	Potential Failure Effects	SEVERITY	Potential Causes	OCCURRENCE	Current Controls	DETECTION	RPN	Actions Recommended	Resp.	Actions Taken	SEVERITY	OCCURRENCE	DETECTION	RPN
What is the process step and Input under investiga-tion?	In what ways does the Key Input go wrong?	What is the impact on the Key Output Variables (Customer Requirements)?		What causes the Key Input to go wrong?		What are the existing controls and procedures (inspection and test) that prevent either the cause or the Failure Mode?			What are the actions for reducing the occurrence of the cause, or improving detection?		What are the completed actions taken with the recalculated RPN?				
								0							0
								0							0
								0							0
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								0							

System/process/product Elements analyzed

System/process/product Elements analyzed

Potential Failure Mode effects and serverity S

Potential Failure Mode causes and probability P

Assessed current controls and detectability D

RISK EVALUATION and priority

prevention/mitigation action plan

RISK EVALUATION and priority

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BEST PRACTICIES

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Tools/Template

Area	System	Template
Collaboration	• Teamsite- SharePoint	
Planning	• TTP • RACI • ESH • Planisware/ Ms Project	Tech Transfer Plan RACI matrix Ms Project Tech Transfer
Gate reviews	• Gate 1, 2,3 ,4	Gate 1 review - Go/No go with transfer Gate 2 review - Go/No go to proceed with Validation PV1 Gate 3 review - Go/No go to continue validation PV2+3 Gate 4 review - Go/No go with submission
Risk assessment	• Risk/Gap assessment High level, FMEA	Gap/Risk assessment high level FMEA
Agenda/Minutes	• Agenda & Minutes	Agenda/Minutes Action list
Lessons learned	• Lesson learned template	Lessons learned and handover

Thoughts to Consider

DO

- Maintain clear and open communication between all parties
- Gather the right information
- Review the history to help find issues
- Review the regulatory compliance status – any variations?
- Develop contingency plans
- Plan for risk
- Understand your variability and control it in your process
- Process aligned to the formulation
- Well defined and technically justified critical performance parameters

DON'T

- Make assumptions without question
- Change parameters without adequate support
- Take too many risks, and then only with a thought out plan

Вопросы?

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