



Management of product transfer projects

Богдан Терлецкий

Директор проектов дирекции по производству Abbott в России

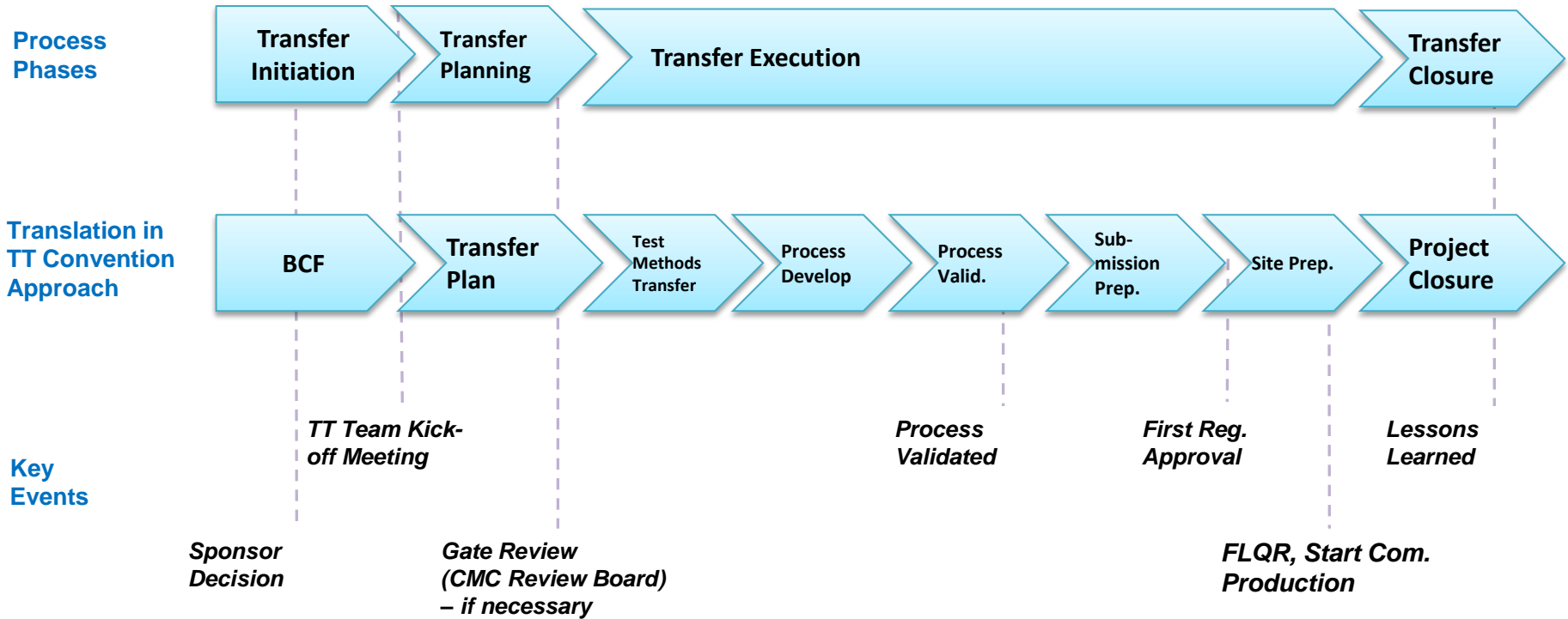
Content

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

TECHNOLOGY TRANSFER

PROJECT STRUCTURE

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

Transfer
Planning

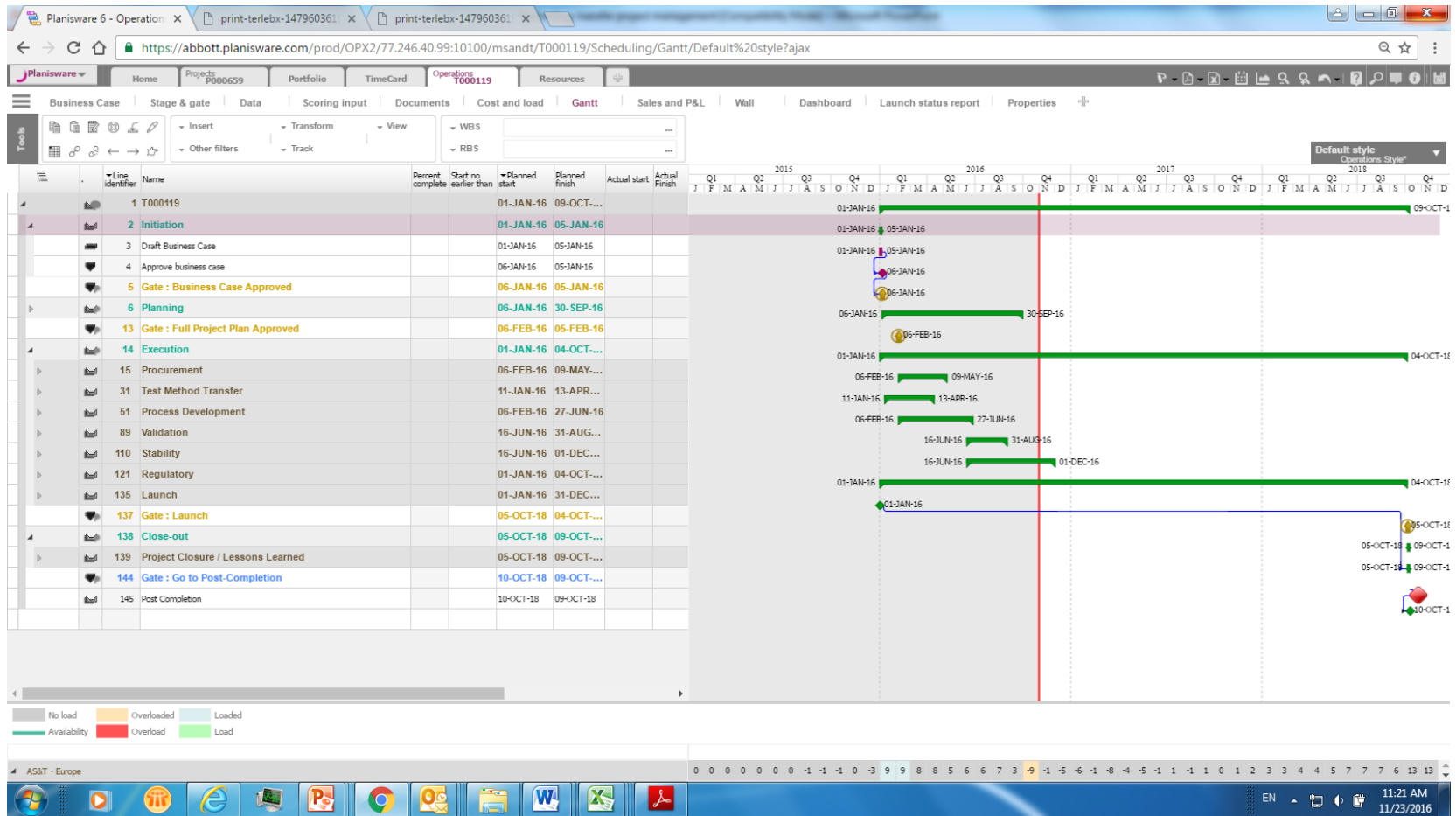
Objective

- 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)

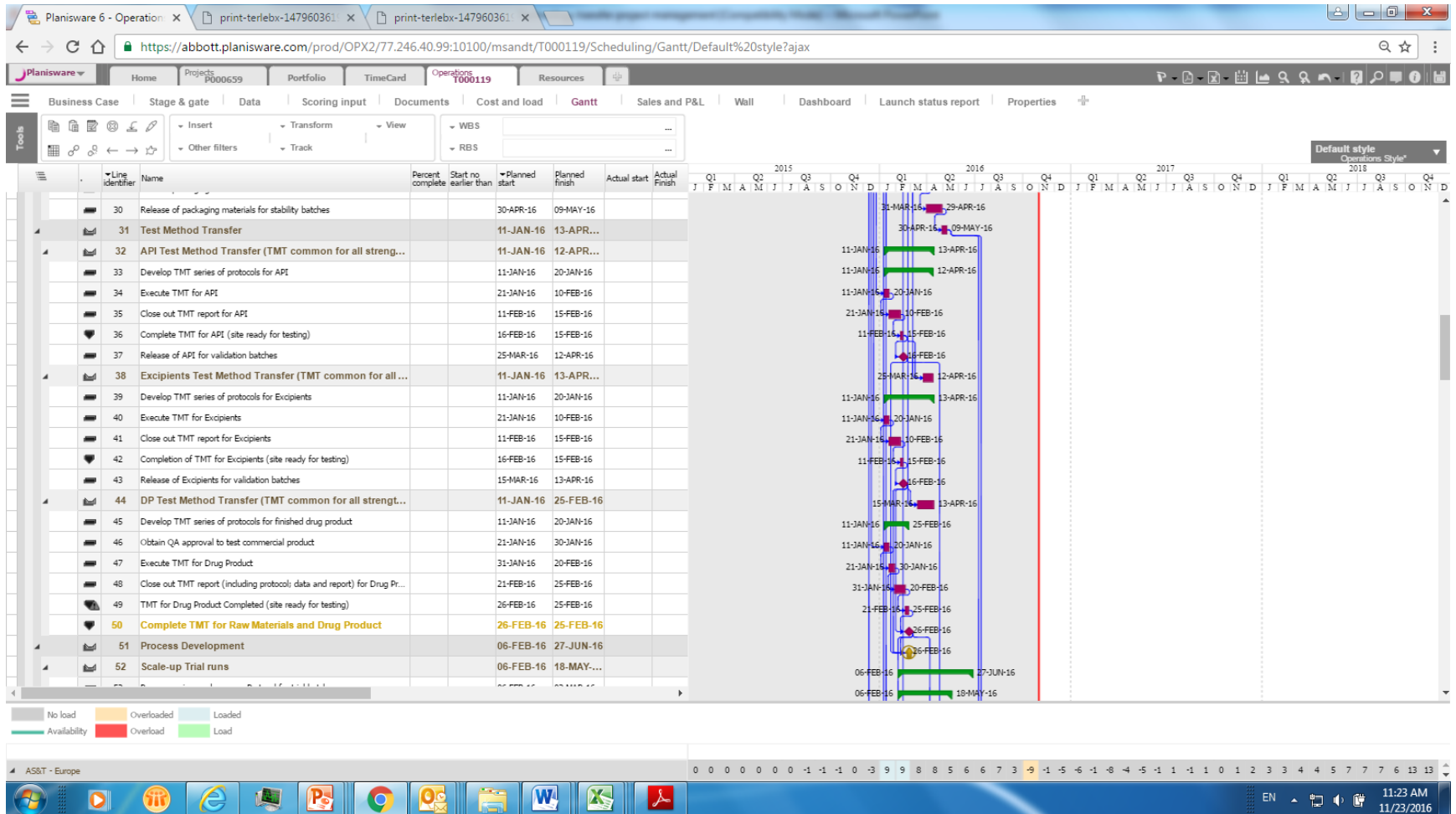
Key Activities

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



Internal resource planning, example

The screenshot displays the Planisware 6 software interface, showing a resource planning table for a project titled "Product transfer to the new manufacturing site". The table lists various tasks and the resources assigned to them, including Total load, Start date, Finish date, and Required skills.

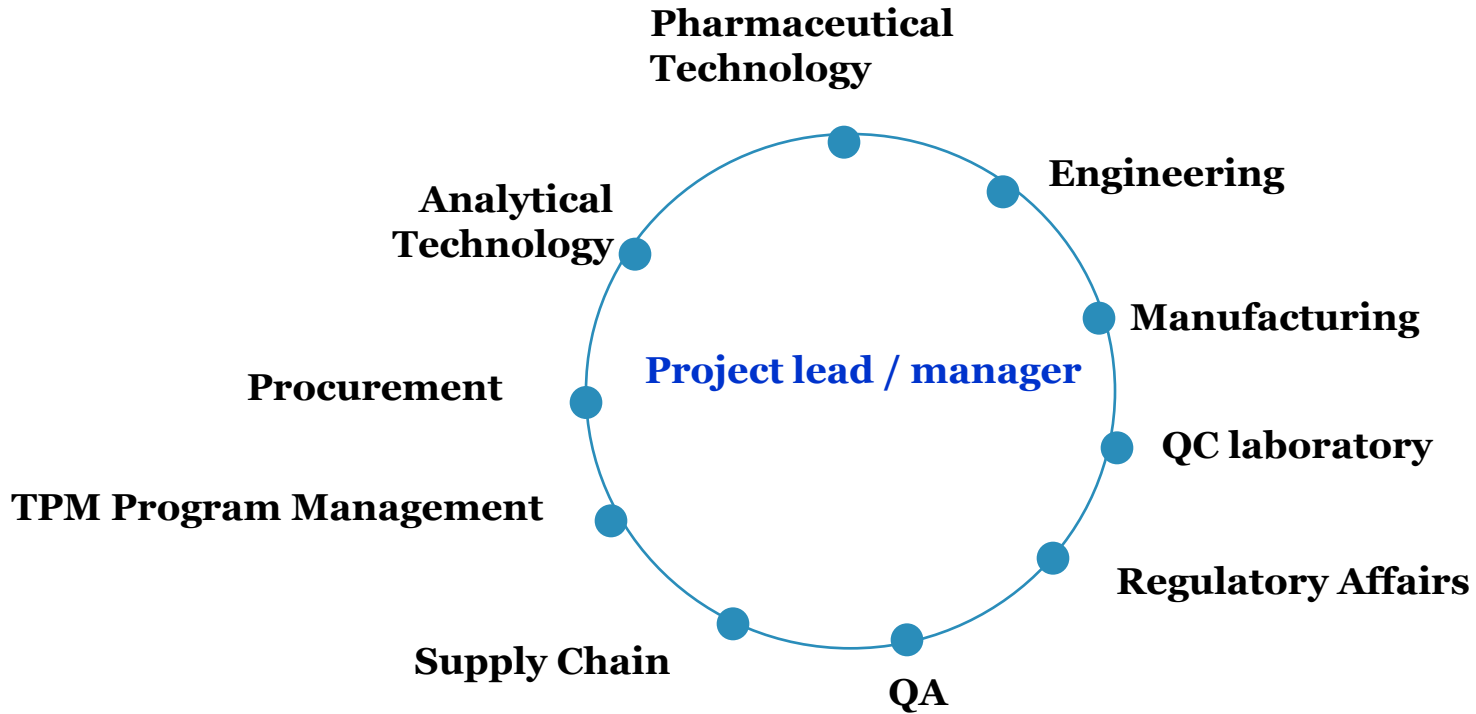
Resource	Total load	Start date	Finish date	Required skills	Finish date	Required skills	Duration
Product transfer to the new manufacturing site							
Planning							
PM-Europe	70	01-OCT-16					
PS&T - Europe	120	01-OCT-16	30-SEP-16		30-SEP-16		
AS&T - Europe	88	01-OCT-16	30-SEP-16		30-SEP-16		
Tech Transfer Plan							
Hold Team Kick off meeting (high level scope)							
PS&T - Europe	8	08-JAN-16	08-JAN-16		08-JAN-16		1d
PM-Europe	8	08-JAN-16	08-JAN-16		08-JAN-16		1d
AS&T - Europe	8	08-JAN-16	08-JAN-16		08-JAN-16		1d
Hold Team Meeting to review gap/risk/planning (F2F)							
PS&T - Europe	30	08-JAN-16	10-JAN-16		10-JAN-16		1d
PM-Europe	30	08-JAN-16	10-JAN-16		10-JAN-16		1d
AS&T - Europe	24	08-JAN-16	10-JAN-16		10-JAN-16		1d
Write review and approve Tech Transfer Plan (TTP)							
PS&T - Europe	44	09-JAN-16	05-FEB-16		05-FEB-16		20d
AS&T - Europe	20	09-JAN-16	05-FEB-16		05-FEB-16		20d
PM-Europe	92	09-JAN-16	05-FEB-16		05-FEB-16		20d
Execution							
Process Development							
Commercial Scale Engineering Batch (potentially to become Validation Batch)							
PM-Europe	143	09-MAY-16	27-JUN-16		27-JUN-16		36d
PS&T - Europe	82	09-MAY-16	27-JUN-16		27-JUN-16		36d
Manufacture Engineering Batch							
PS&T - Europe	60	03-JUN-16	15-JUN-16		15-JUN-16		9d
Validation							
PM-Europe	141	16-JUN-16	31-AUG-16		31-AUG-16		55d
Process Validation							
Validation Protocol Runs							
PS&T - Europe	13	16-JUN-16	23-JUN-16		23-JUN-16		6d
Validation Execution							
PS&T - Europe	28	28-JUN-16	28-AUG-16		28-AUG-16		44d
Execute PV#1							
PS&T - Europe	40	28-JUN-16	02-JUL-16		02-JUL-16		4d
Execute PV #2 #3 (Encapsulation or Tableting; Coating)							
PS&T - Europe	60	17-JUL-16	24-JUL-16		24-JUL-16		5d
Draft review and approve Validation Report							

External resource planning, example

The screenshot displays the Planisware 6 software interface, specifically the 'Cost and load' section. The browser address bar shows the URL: <https://abbott.planisware.com/prod/OPX2/77.246.40.99:10100/msandt/T000119/Cost%20and%20load/Distributed%20cost?ajax>. The interface includes a navigation menu with options like Business Case, Stage & gate, Data, Scoring input, Documents, Cost and load, Gantt, Sales and P&L, Wall, Dashboard, Launch status report, and Properties. A toolbar at the top right contains various icons for document management. Below the navigation is a 'Costs notes' section with a rich text editor. The main area is a spreadsheet titled 'Distributed cost' showing cost accounting data for 2016 and 2017. The spreadsheet columns represent months (J, F, M, A, M, J, J, A, S, O, N, D) for each quarter (Q1, Q2, Q3, Q4) across the two years. The rows list various cost categories such as 'Operations Cost accounts', 'BE studies, Tox/Pre-Clinical stu...', 'ICH, Excursion, Stress', 'API, Excipient, Packaging mater...', 'Batch manufacturing, paper wo...', 'Spec/IPC/PSD/TMT', 'Bio waiver, Regulatory Strategy, ...', 'COA, Samples, Translation', 'Mold, tooling, equipment rentin...', 'Travel, site visit, DD, reporting', 'Operations Other', 'CAPEX', and 'Inventory at risk'. The 'Total sum' column on the left indicates the total cost for each category, with values like 110,000.00 for Operations Cost accounts and 10,000.00 for Mold, tooling, equipment rentin... The spreadsheet shows numerical values for specific months, such as 20,000.00 for Q4 2016 and 30,000.00 for Q1 2017.

Type of cost	Cost unit	Total sum	2016 Q1	2016 Q2	2016 Q3	2016 Q4	2017 Q1	2017 Q2	2017 Q3	2017 Q4
Operations Cost accounts	EUR	110,000.00				20,000.00				
BE studies, Tox/Pre-Clinical stu...	EUR	0.00								
ICH, Excursion, Stress	EUR	80,000.00					30,000.00			
API, Excipient, Packaging mater...	EUR	20,000.00				20,000.00				
Batch manufacturing, paper wo...	EUR	0.00				20,000.00				
Spec/IPC/PSD/TMT	EUR	0.00								
Bio waiver, Regulatory Strategy, ...	EUR	0.00								
COA, Samples, Translation	EUR	0.00								
Mold, tooling, equipment rentin...	EUR	10,000.00				10,000.00				
Travel, site visit, DD, reporting	EUR	0.00				10,000.00				
Operations Other	EUR	0.00								
CAPEX	EUR	0.00								
Inventory at risk	EUR	0.00								

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

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

TECHNOLOGY TRANSFER

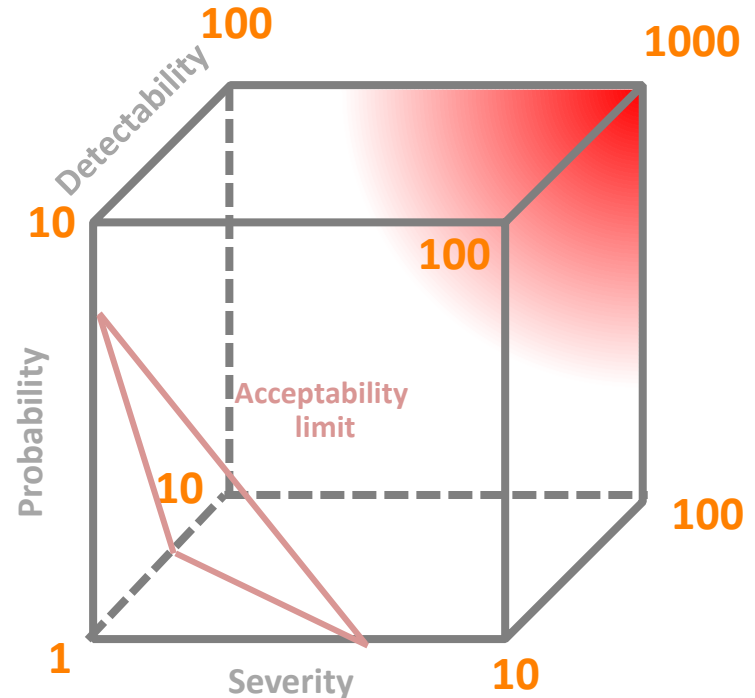
RISK MANAGEMENT

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)

$$\mathbf{RPN = P \times D \times S}$$

Item RPN range
(1-1000)

Failure occurrence probability
(score 1-10)

Detection probability
(score 1-10)

Impact severity (damage)
(score 1-10)

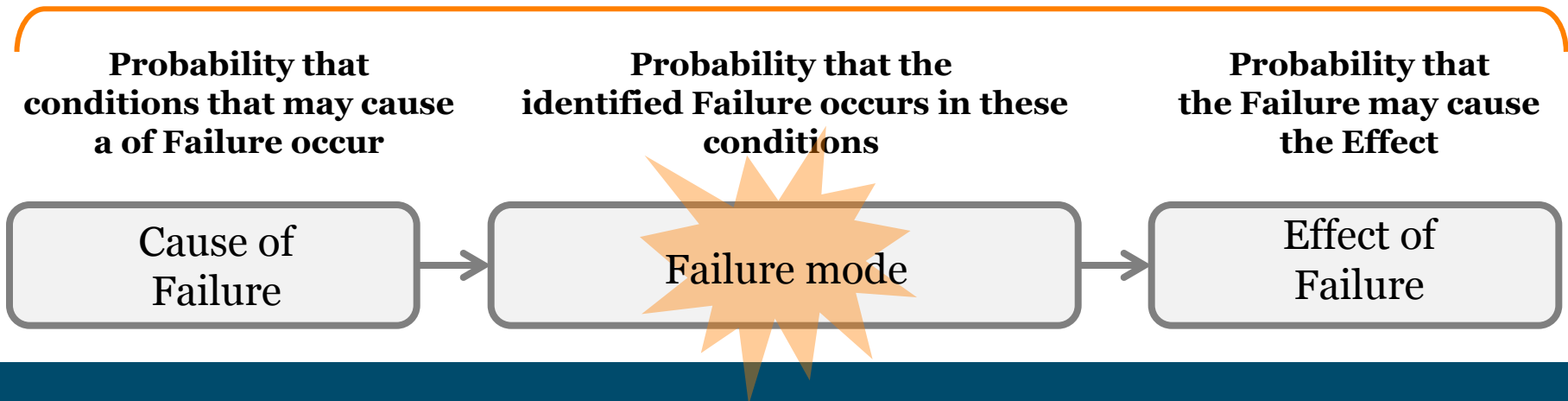
Probability that the whole causal chain cause-failure-effect may occur

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

Probability

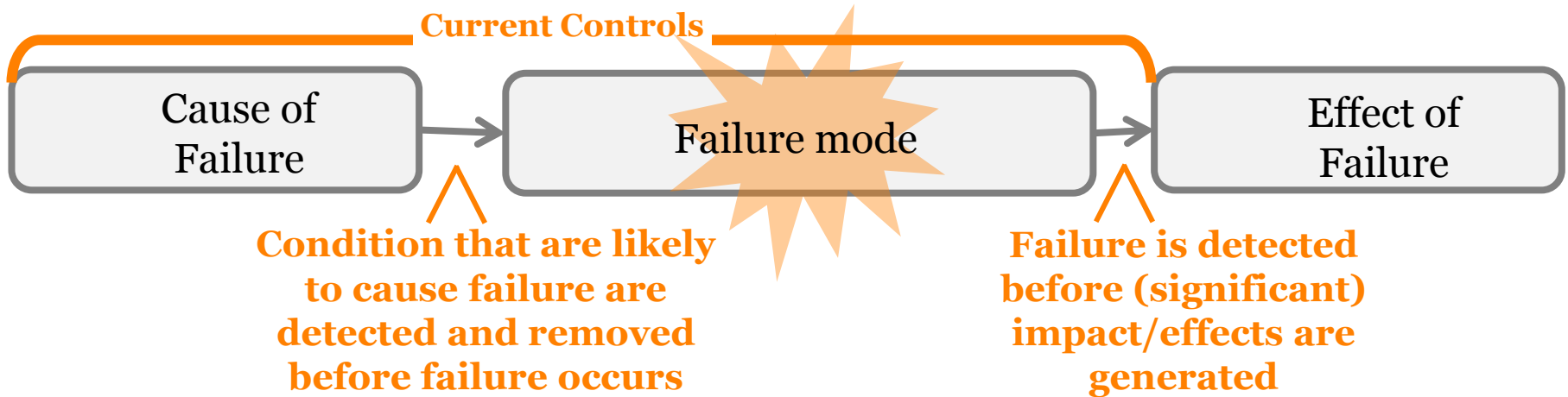
- **Estimates the probability that the entire sequence Cause/Failure/Effect may occur.**
- Probability estimation may involve:
 - quantitative evaluation of historic occurrences
 - **qualitative evaluation according to subjective experience, expertise**

Probability that the Effect of Failure Mode occurs



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;

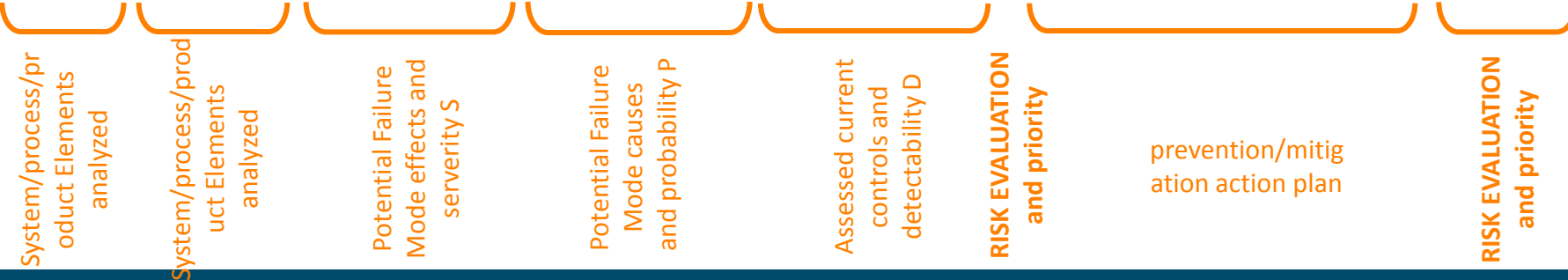


FMEA deliverable

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

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

Process Step / Input	Potential Failure Mode	Potential Failure Effects	S E V E R I T Y	Potential Causes	O C C U R R E N C E	Current Controls	D E T E C T I O N	R P N	Actions Recommended	Resp.	Actions Taken	S E V E R I T Y	O C C U R R E N C E	D E T E C T I O N	R P N
What is the process step and input under investigation?	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
								0							0
								0							0
								0							0



TECHNOLOGY TRANSFER

BEST PRACTICES

Tools/Template

Area	System	Template
Collaboration	<ul style="list-style-type: none"> Teamsite- SharePoint 	
Planning	<ul style="list-style-type: none"> TTP RACI ESH Planisware/ Ms Project 	Tech Transfer Plan RACI matrix Ms Project Tech Transfer
Gate reviews	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Risk/Gap assessment High level, FMEA 	Gap/Risk assessment high level FMEA
Agenda/Minutes	<ul style="list-style-type: none"> Agenda & Minutes 	Agenda/Minutes Action list
Lessons learned	<ul style="list-style-type: none"> 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?

academy@veropharm.ru