B1

Connecting People, Science and Regulation

PDA Training Course on

Technology Transfer

Project Management & Quality Risk Management

Trainer:
Mirko Gabriele, Patheon

Firenze, 21 Ottobre 2015

Diapositiva 1

B1 In general I would suggest to write acronyms out at the beginning of the course here PM and QRM

Backes; 13/06/2014

Agenda

1. **Welcome and introduction (09:00 – 10:00)**
   a. Attendees presentation
   b. Scope of the training
   c. Agenda for the day
2. **Technology Transfer (10:00 – 11:00)**
   a. Definition
   b. Opportunities along product lifecycle
   c. TT process
   d. Prj management
3. **Q/A Section (11:00 – 12:00)**

LUNCH BREAK

4. **QRM in TT and QRM application (14:00 – 15:00)**
   a. PMCO program
   b. ICH Q9 brief introduction
   c. Why QRM in TT
   d. How QRM in TT
   e. TR 65

COFFEE BREAK

5. **Technology Transfer Approaches - let's discuss and benchmark**

Attendees Presentation

Technology Transfer Manager

– Ferentino Site, *Responsible for TT project managers & coordinators*

- Pharmaceutical Chemist by training, got my degree in Rome
- Executive MBA in Pharma Business Administration
- Since June 2008 working for Patheon
- Previously R&D Scientist in Chemi Spa (Italfarmaco Group)

My career in Patheon started in 2008 as Tech Transfer Project Manager, followed by Technical Business Manager experience.

The part that I like more about my job is that "*We can always make the difference for our stakeholders*"

I love scuba-diving, playing guitar, reading fantasy books and business/financial newspaper.

Two sentences summarize my professional approach:

- *"Fabrum esse suae quemque fortunae"* adding to the original quote *"good teamwork helps a lot*!"
- *"Ad maiora semper"*

B2

Attendees Presentation

Diapositiva 4

B2 Please announce here:
Particpants are kindly invited to fill the evaluation forms out after the training course (they will be placed in the training course binder
Backes; 13/06/2014

Why joining the training?

- Incredible **increase** of number of **Technology Transfer projects** (TTP) in the pharmaceutical environment, both internal & external and consequent increase of attention on Technology Transfer (TT) handling by Authorities;
- Project **complexity** is growing day by day;
- **Risks of failure** is always high;
- **Quality Risk Management (QRM) & Project Management (PM)** skills and knowledge are fundamental for success!

Morning Topics

1. Technology Transfer – Definition and Main Concepts
2. Opportunities Along Product lifecycle
3. Planning and Social Intelligence
4. Tools for planning
5. Technology Transfer Project Management

Morning Topics

1. Technology Transfer – Definition and Main Concepts
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B4

Some Useful Terminology

- **Technology Transfer (TT)**
  - The transfer of product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realization (ICH Q10).
  - Technology Transfer Project (TTP) is a set of planned and controlled actions based on well-defined acceptance criteria needed to transfer a technology from a sending unit (SU) to a receiving unit (RU).
- **Sending Unit (SU)**
  - The involved disciplines at an organization from where a designated product, process or method is expected to be transferred.
- **Receiving Unit (RU)**
  - The involved disciplines at an organization where a designated product, process or method is expected to be transferred.
- **Risk Management (RM)**
  - Risk is combination of severity of harm and probability of occurrence (ICH Q9).
  - Applicable to Technology Transfer Projects – harm is event that could delay/stop a project
- **Comparability**
  - The demonstration that the quality attributes are highly similar and that the existing knowledge is sufficiently predictive to ensure that any differences in quality attributes have no adverse impact upon safety or efficacy of the drug product (ICH Q5E).

Diapositiva 8

B4 Suggestion of a defition slide:
but please modifie the definition as needed
Backes; 13/06/2014

B3

Technology Transfer

Definition and main concepts

A process for conceiving and implementing a new/novel application for an existing technology *(Reisman, 1989)*

The technology transfer consists of actions taken ….to realize the quality as designed during the manufacture (*NIHS, 2005*)

A logical procedure that controls the transfer of an established process together with its documentation and professional expertise to a site capable of reproducing the process and its support functions to a predetermined level of performance *(WHO Guideline on transfer technology, 2008)*

Diapositiva 9

B3 Backes; 13/06/2014

Technology Transfer

Definition and main concepts

The Technology Transfer Project (TTP) is defined as a set of planned and controlled actions, based on well-defined acceptance criteria needed to transfer a technology from a sending unit (SU) to a receiving unit (RU).

The Technology Transfer implies four main topics:

- Technical knowledge
- Documentation management
- Project management
- Personnel training and skills

PDA – PMCO Program – Technical Report N.65

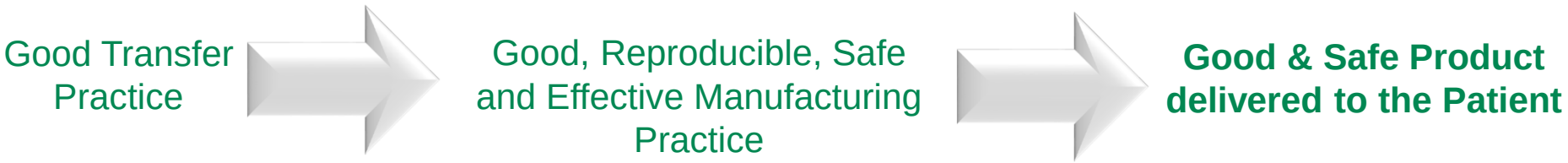
Technology Transfer

Definition and main concepts

The Technology Transfer Project (TTP) is defined as a set of planned and controlled actions, based on well-defined acceptance criteria needed to transfer a technology from a sending unit (SU) to a receiving unit (RU).

Technology = Drug

Technology Transfer Projects must have product quality, product safety and process performance as primary objectives.



Technology Transfer

Definition and main concepts

The Technology Transfer Project (TTP) is defined as a set of planned and controlled actions, based on well-defined acceptance criteria needed to transfer a technology from a sending unit (SU) to a receiving unit (RU).

Scope of the project must be clearly stated and agreed upon within the team and a structured plan needs to be developed.

Project is a sum of non-repetitive activities which are:

- addressed to a particular goal
- have to be performed in a defined time range
- employ defined resources
- and are managed by a team.

Technology Transfer

Definition and main concepts

5 main steps!

1. Planning

a. Definition of Project Scope and Rationale and the overall project plan

b. Technology and Knowledge clearly stated

c. Delvierables defined

d. Control philosophy agreed

e. Risks evaluated and mitigation plan defined

Technology Transfer

Definition and main concepts

5 main steps!

2. Process Readiness

a. Control and Achieve the readiness set for the poject

b. Each TT phase and milestones has its own readiness

c. Stage/Gate step along the project exeution

d. Process changes tracking and handling

e. Training and expertise challenge

Technology Transfer

Definition and main concepts

5 main steps!

3. Implementation and Qualification

a. Facility modification
b. Equipment installation and modification
c. Analytical transfer
d. Cleaning and environmental monitoring
e. TT batches
f. Process Validation

Technology Transfer

Definition and main concepts

5 main steps!

4. Licensing & Manufacturing

a. Regulatory submission

b. Monitoring of the manufacturing batches

Technology Transfer

Definition and main concepts

5 main steps!

5. Project Closure

a. Continuous improvement

b. Lesson learned

Technology Transfer

Definition and main concepts

- Applications of technology transfer must be GMP based and rely on well-documented knowledge.
- Specific acceptance criteria (objectives), must be defined in advance.
- The scope of the TTP must be clearly stated and agreed upon by the TTP team.
- Transfer drivers and control philosophies should be put in place and agreed between Sending unit and Receiving Unit

Technology Transfer

Definition and main concepts

Success Criteria?

"You can tell pharmacy we finally have three batches of on-spec product."

Morning Topics

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2. Opportunities Along Product lifecycle
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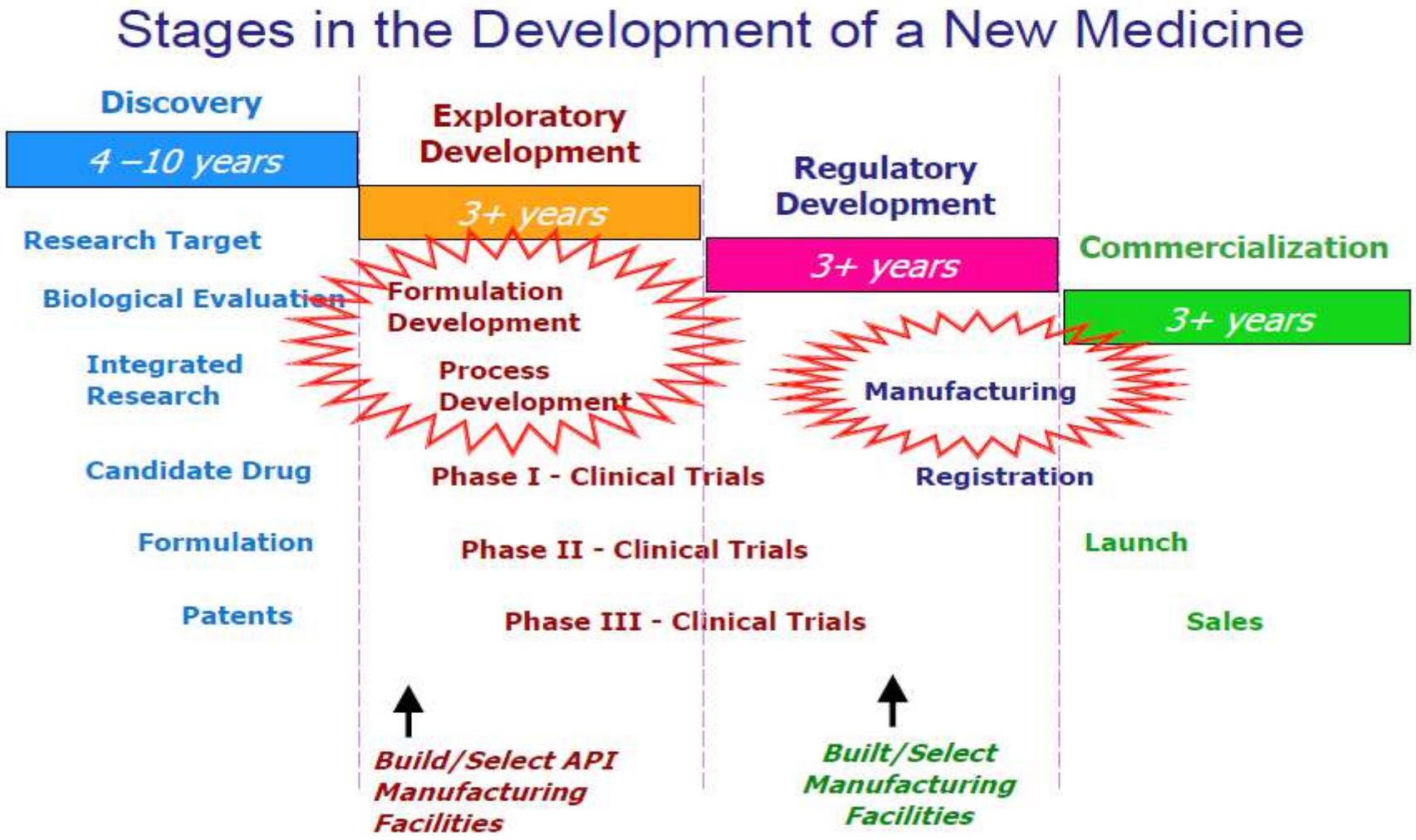
4. Tools for planning
5. Technology Transfer Project Management

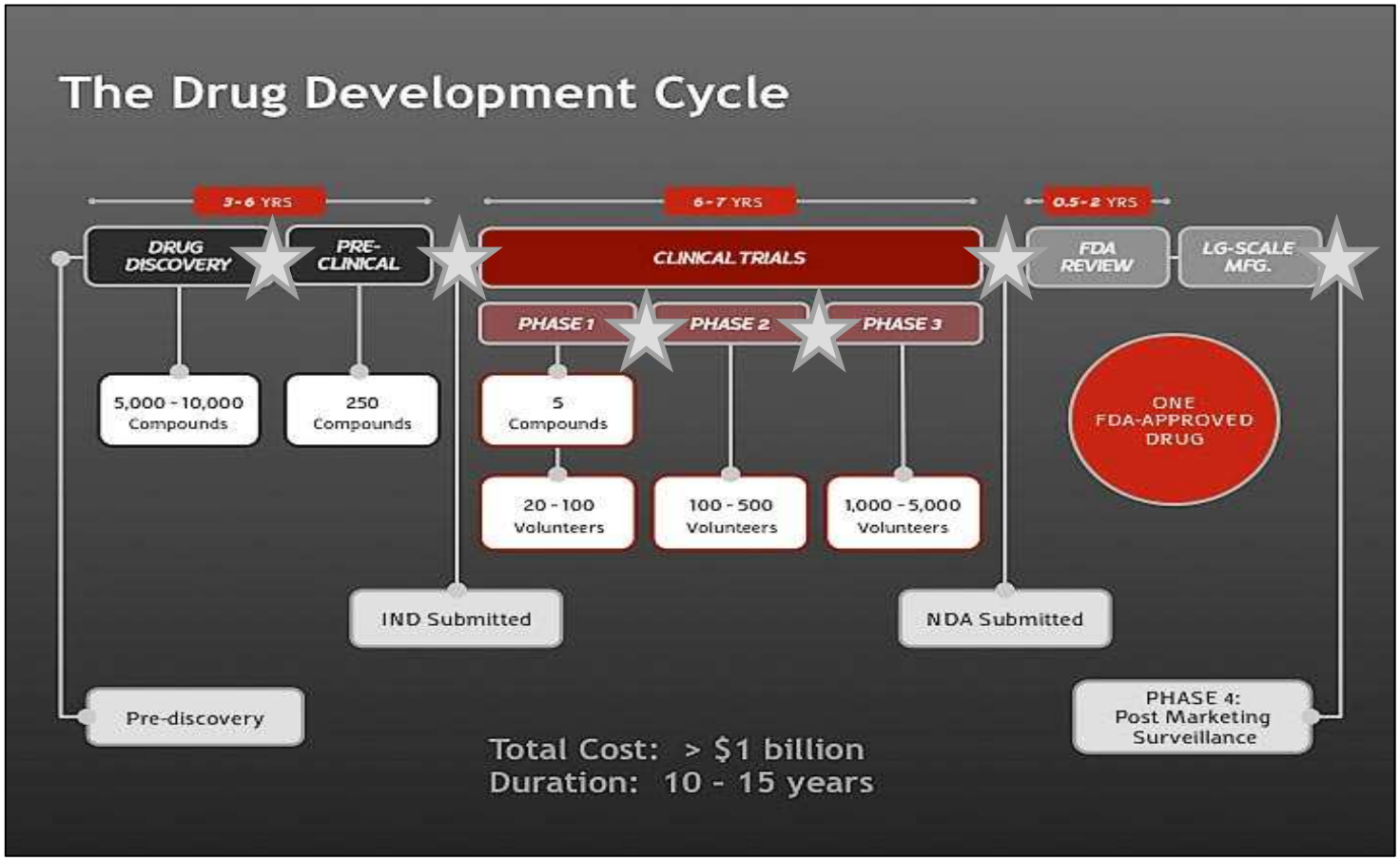
Technology Transfer

Definition and main concepts



Technology Transfer

Definition and main concepts



Technology Transfer

Definition and main concepts

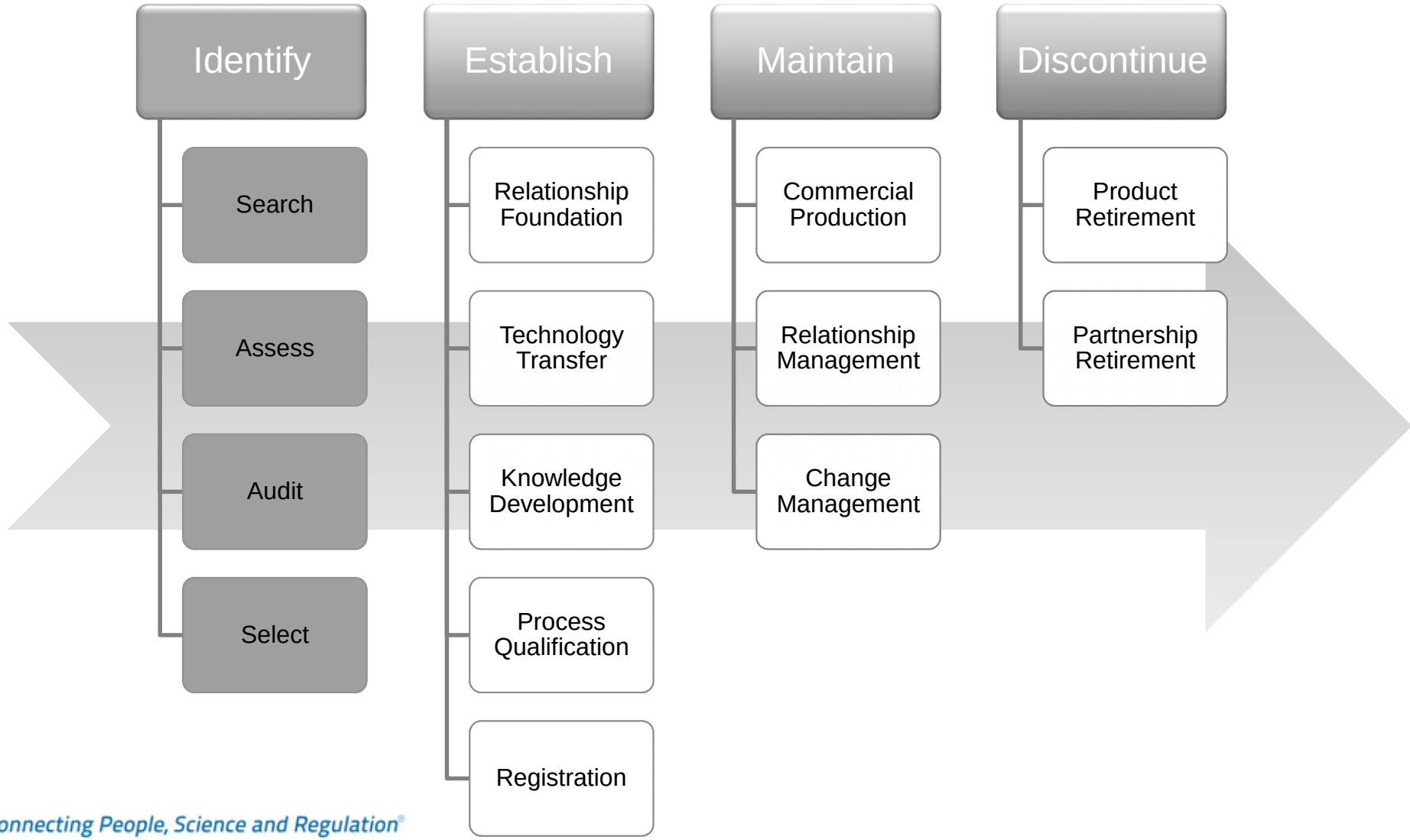
Different pharmaceutical Technology Transfer Project contexts can be managed; each with specific peculiarities; assuming the technology to be transferred is the drug manufacturing process, several possibilities arise:

- *Development to clinical phase TTP*
- *Clinical Phase to Commercialization TTP*
- *Commercial TTP*

- *Intra-company site to site TTP*
- *Inter-company site to site TTP*

Technology Transfer

Definition and main concepts



Technology Transfer

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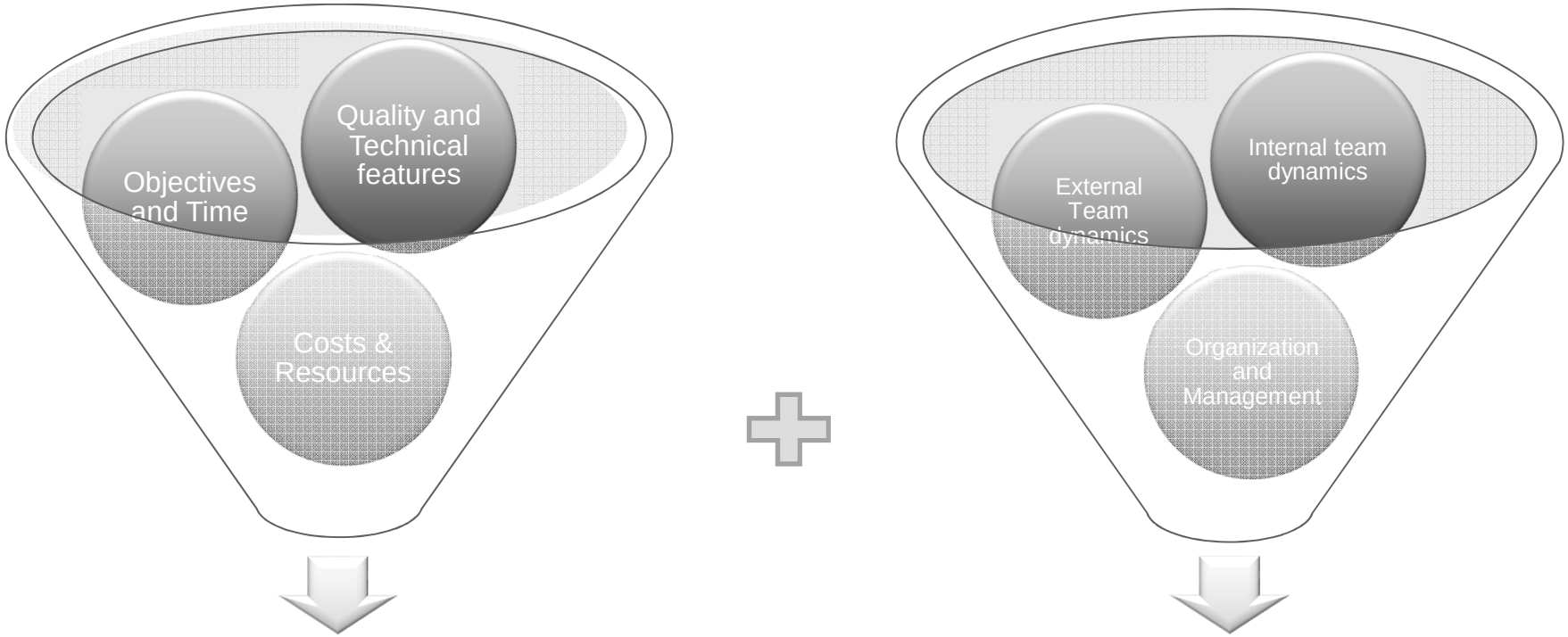
PDA – PMCO Program – Technical Report N.65

Technology Transfer

Definition and main concepts



Planning

Social Intelligence

Technology Transfer

Team not individual!

3.4.2 Multidisciplinary Technology Transfer Project Team

Each pharmaceutical TTP requires the involvement of a well-trained, multidisciplinary team at both the SU and RU. The team needs such soft skills as leadership, effective communication, and pharmaceutical market access principles. The team also needs the following technical proficiencies to drive the team toward a positive outcome:

- Quality assurance
- Quality control
- Manufacturing
- Engineering
- Finance
- Maintenance
- Environment, health, and safety
- Research and development
- Regulatory affairs
- Legal issues
- Project management

Technology Transfer

Team not individual!

Table 3.4.2-1 Technology Transfer Organizational Components

Category of Responsibility	Roles
Administrative/ Regulatory	• Monitor the TTP through gate reviews, and be available for advice and consult • Represent the interests of upper management during the project • Monitor the budget and investment expense forecasts • Serve as liaison with regulatory authorities and other parties involved in the process
Operational	• Transfer and implement the technology being transferred • Transfer the technology from the SU • Implement the technology at the RU • Monitor and coordinate the project • Plan and monitor project development • Suggest corrective actions and contingency plans when needed • Guarantee the performance of planned activities • Engage the teams and gain their active participation • Update management and other stakeholders on project progress • Ensure fulfillment of quality requirements

Technology Transfer

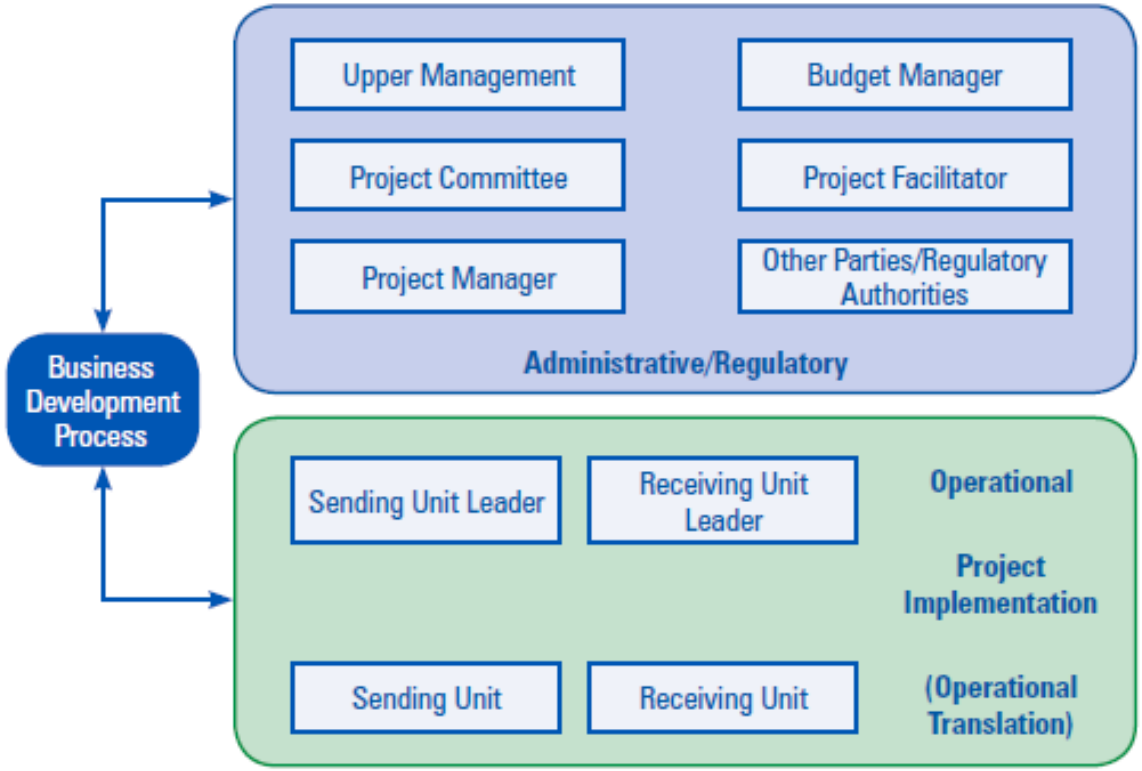
Team not individual!

Table 3.3.1-1 Responsibilities of the SU and RU

Project Stage	SU	RU
Planning	Identify relevant documents	Implement SU-provided documents
Process Readiness	Transfer documents to RU	Organize validation and implementation plans
	Review document implementation at RU	Validate and implement the technology being transferred
	Train RU personnel	Train personnel
Implementation and Qualification	Support RU during validation, start up, and follow-up	Execute start up, evaluate results
	Support RU in failure and gaps evaluation after startup phase	Solve any failure or deviations occurred during startup phase
	Support RU during improvements identification and implementation	Identify potential improvements after start up data evaluation
Closure	Support and sponsor RU in the continuous verification phase after start up	Continuous verification and improvement plan set up

Technology Transfer

Team not individual!

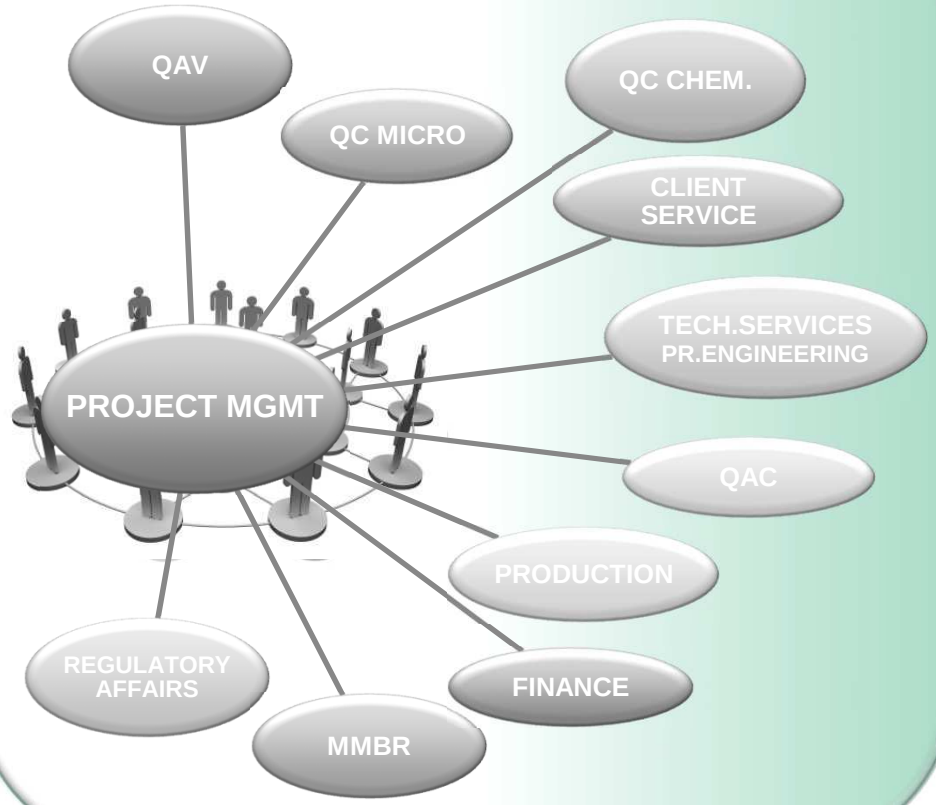


Technology Transfer

Definition and main concepts

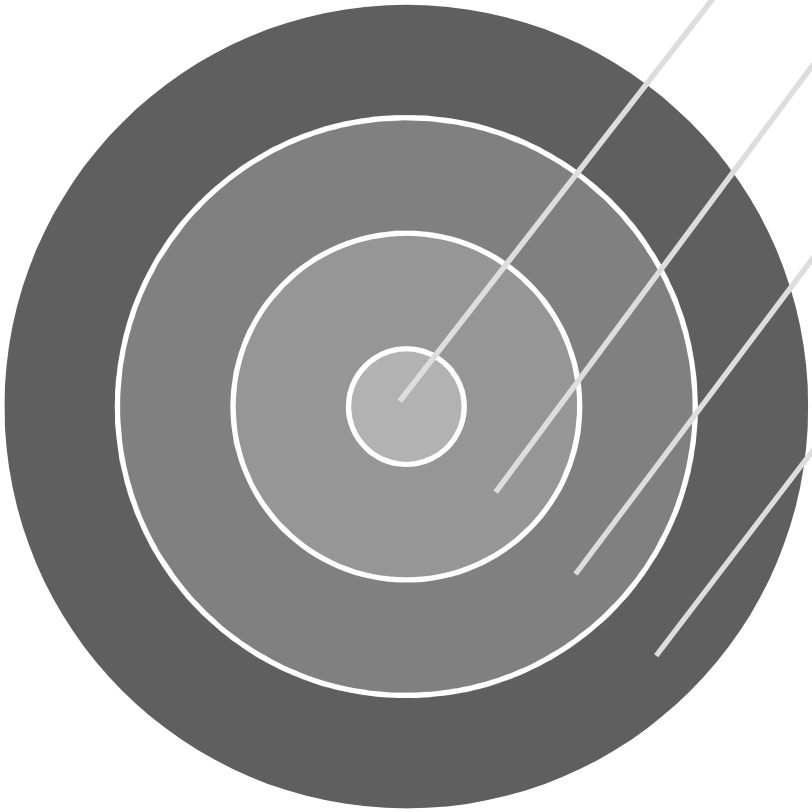
Main External Stakeholder

Internal Stakeholders



Technology Transfer

Definition and main concepts



Personnel training and skills

Documentation management

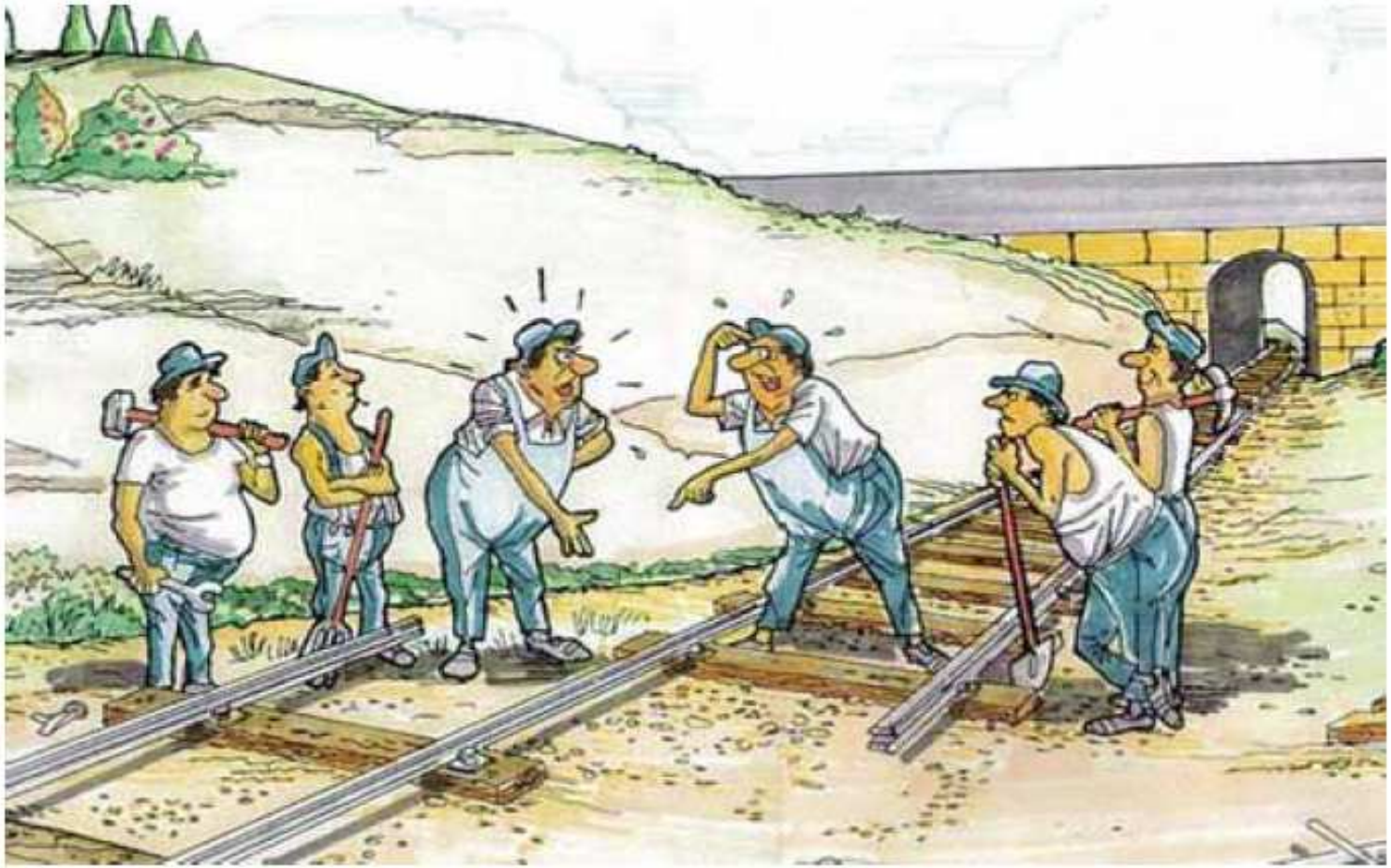
Project management

Technical knowledge

Technology Transfer

Definition and main concepts

Team work, most of the time



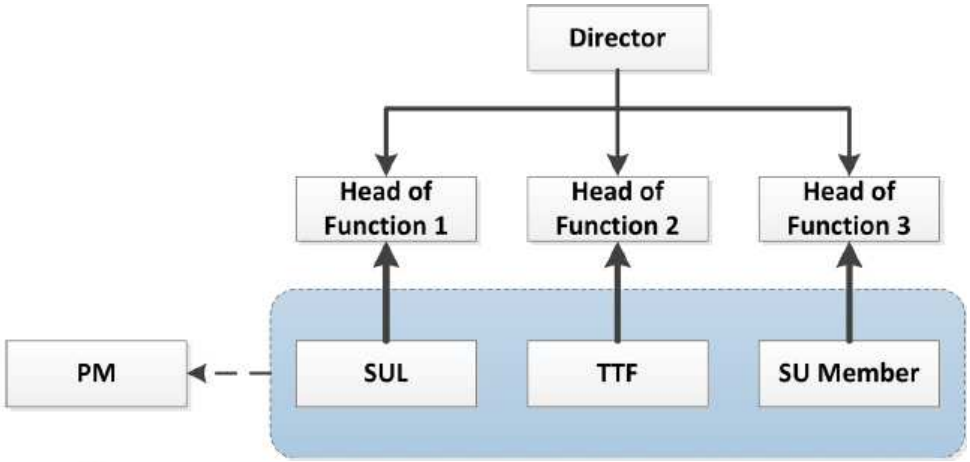
Technology Transfer

Definition and main concepts

An organizational model that identifies the people or groups responsible for each task must be developed and identify which matters are subject to risk-based decisions.

The risk determination of the subjects will provide the group with the necessary awareness of risk.

Often a light matrix approach is preferred. The hierarchical relationship between a project figure (such as an SU leader, technology transfer department, or SU staff member) is maintained in a priority way (bold arrow). This organizational model minimizes the impact of the transfer activities on the routine activities of the units involved in the transfer



Technology Transfer

Definition and main concepts

Each team in the RU and SU should be coordinated by a team leader who is the “owner” of the technology project and is responsible for implementing the technology at the RU or SU (e.g., manufacturing in the case of transfer of an industrial process).

The SU and RU technology team leaders should regularly update the project manager on the progress of the activities, budget use, potential technical or economic issues, and proposed corrective actions.

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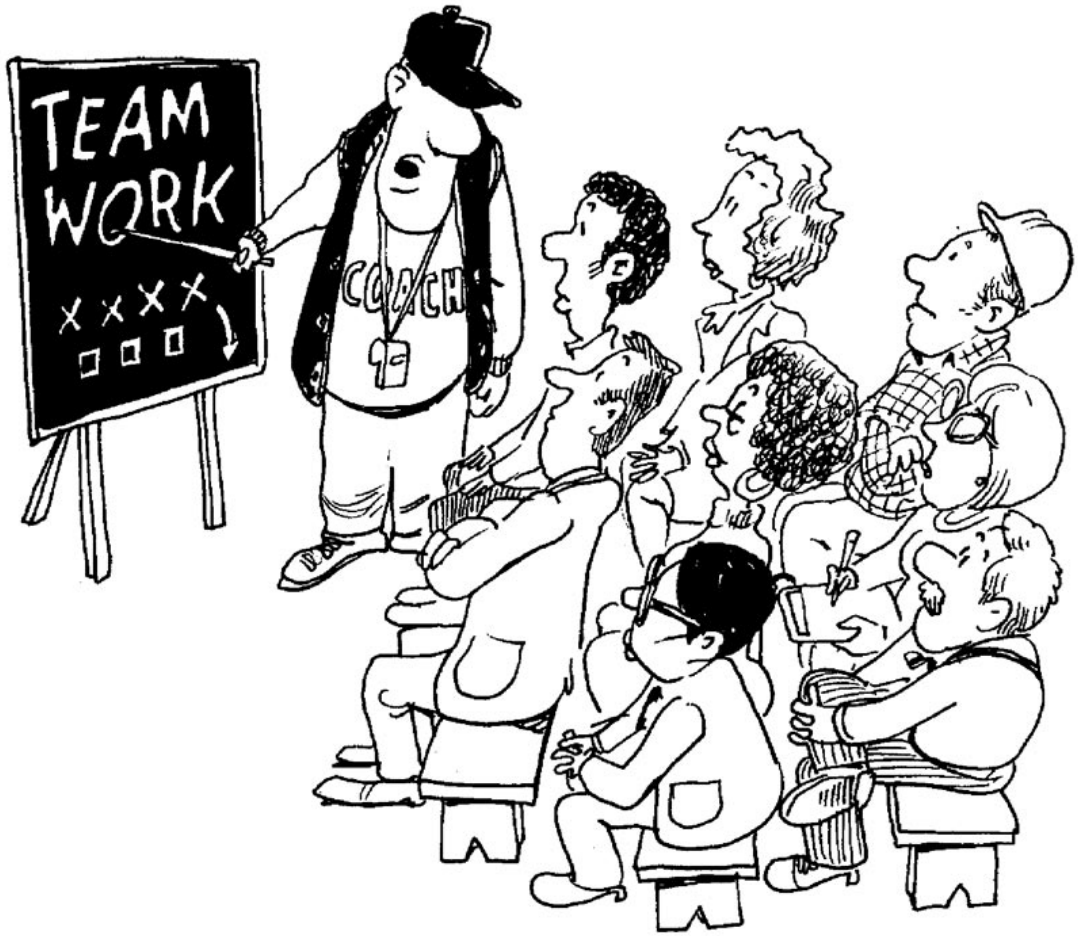
Technology Transfer

Definition and main concepts



Technology Transfer

Definition and main concepts

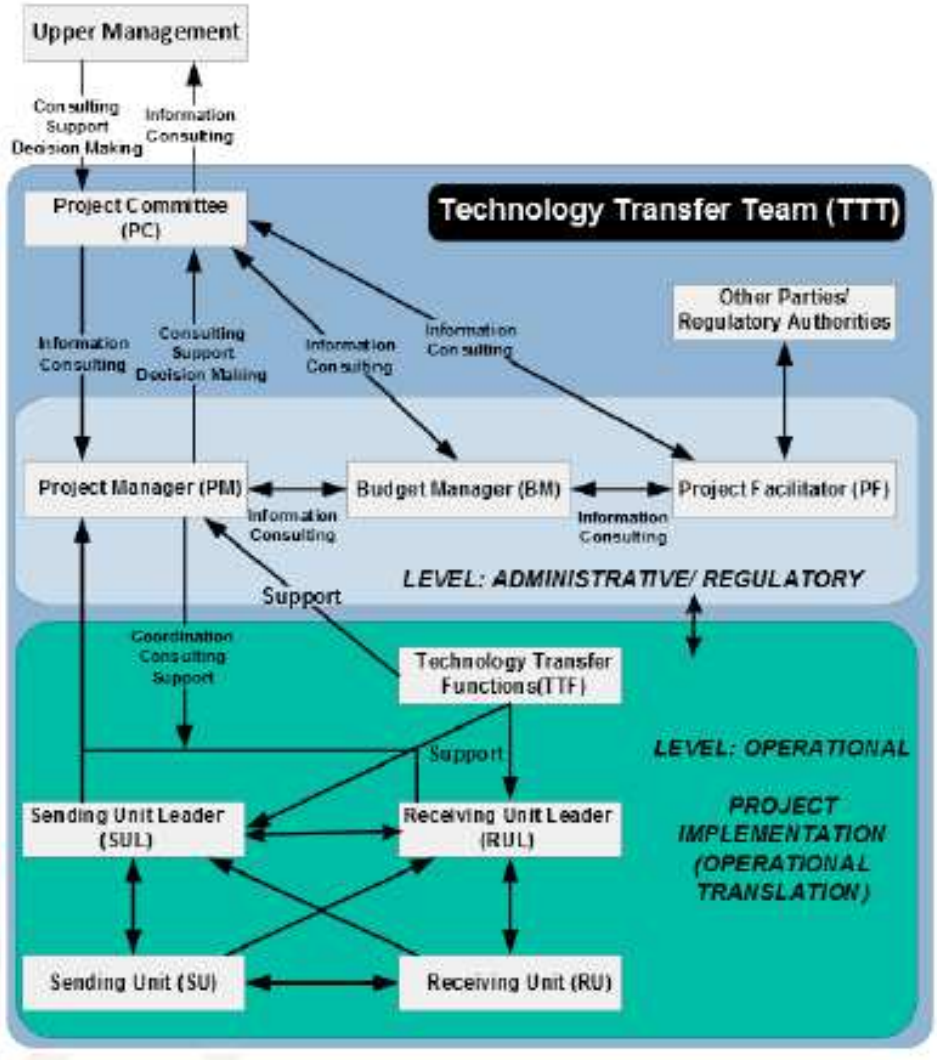
The success of a Technology Transfer is largely related to the **communication** skills and relationship of the Technology Transfer **team** members.

- Open communication between team members
- Effective and timely communication
- Direct communication between subject matter experts

The Technology Transfer leader facilitates meetings and communication between teams

Technology Transfer

Definition and main concepts



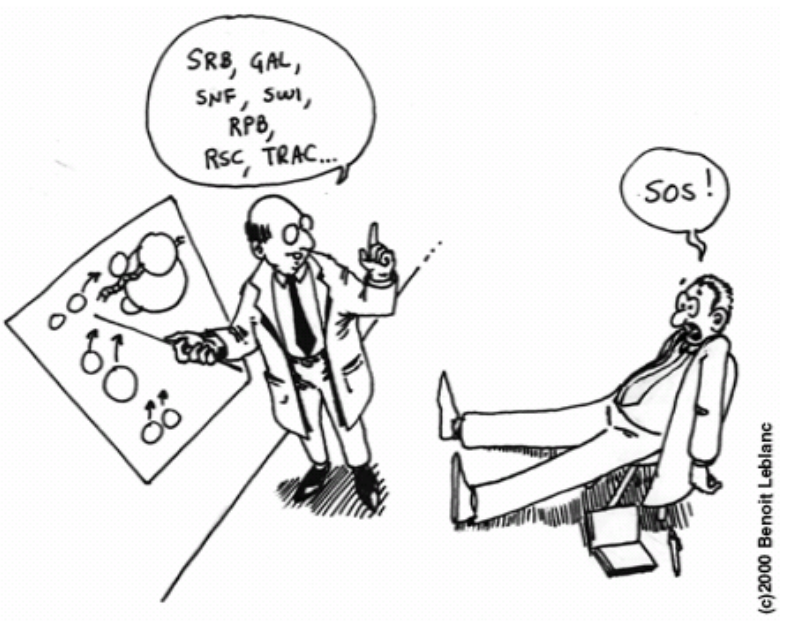
Technology Transfer
Definition and main concepts

1) Weekly Technical Call

2) Weekly Project Management Call

3) Monthly Stirring Committee

4) Business Review meetings



Cultural / organizational differences to be considered and assessed!

Morning Topics

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Technology Transfer

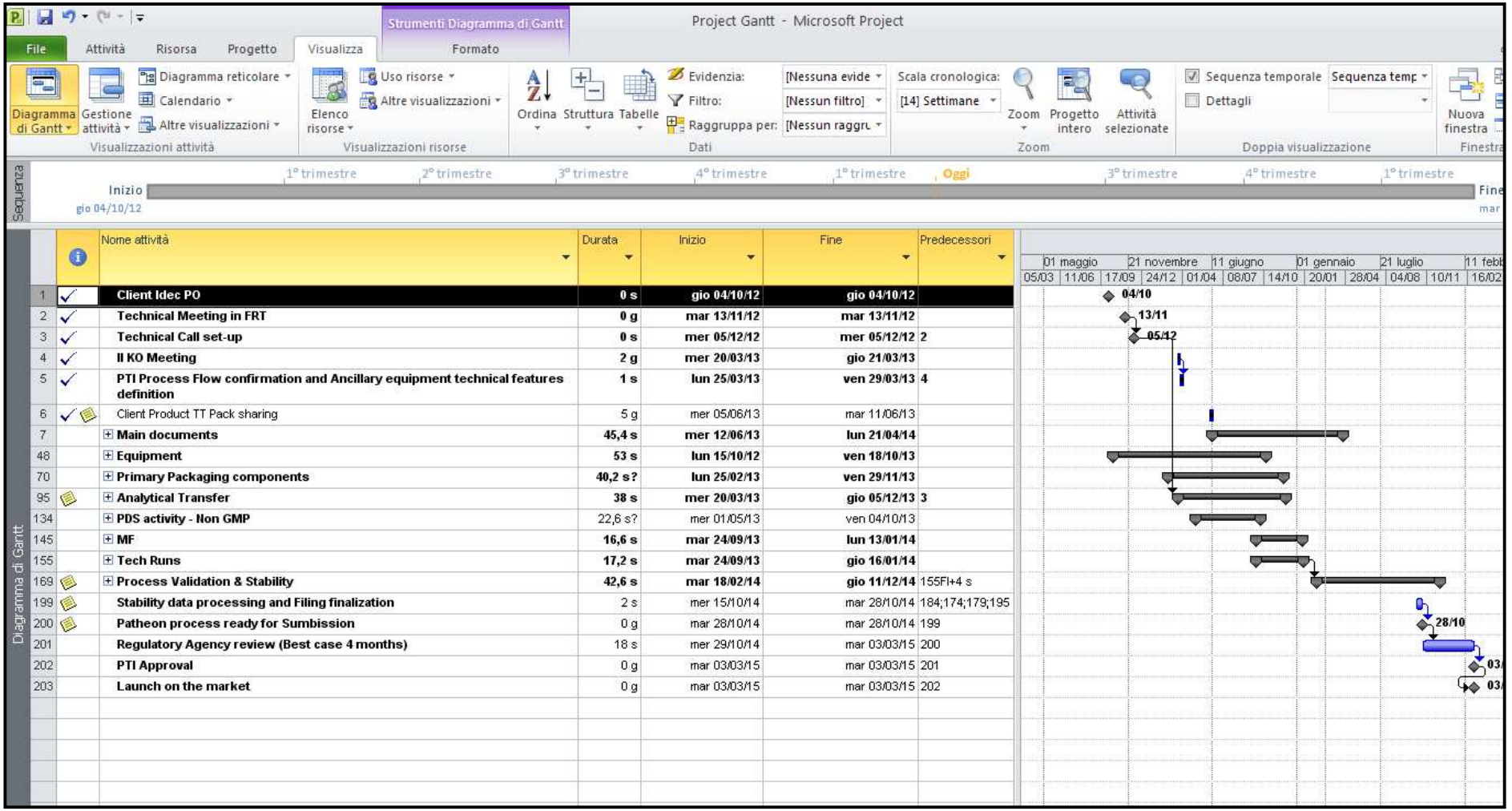
Definition and main concepts

- Project Gantt
- Action List
- Decision List
- Risk Register
- Activities completion tracking

Define scope, plan, execute and track

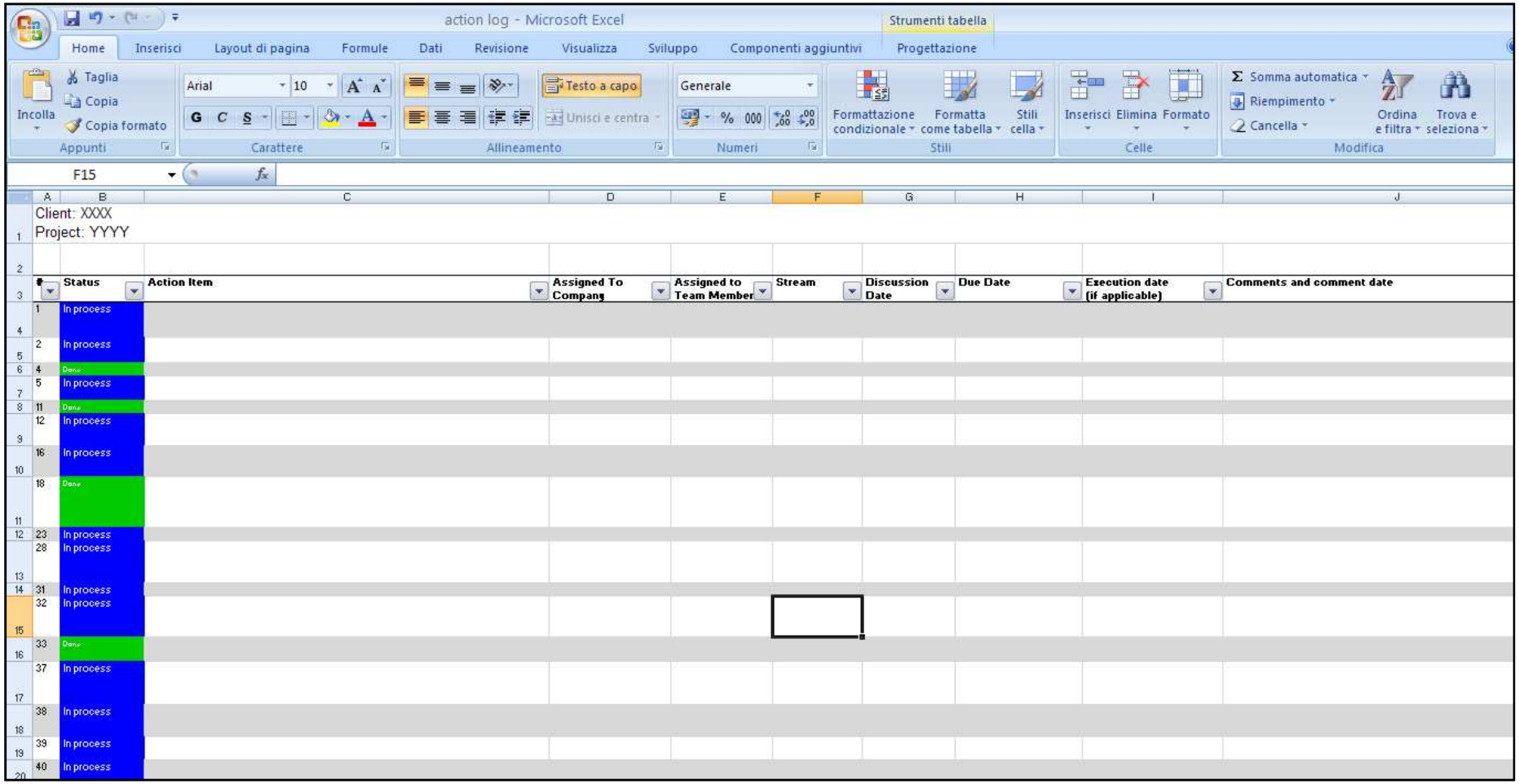
Technology Transfer

Definition and main concepts



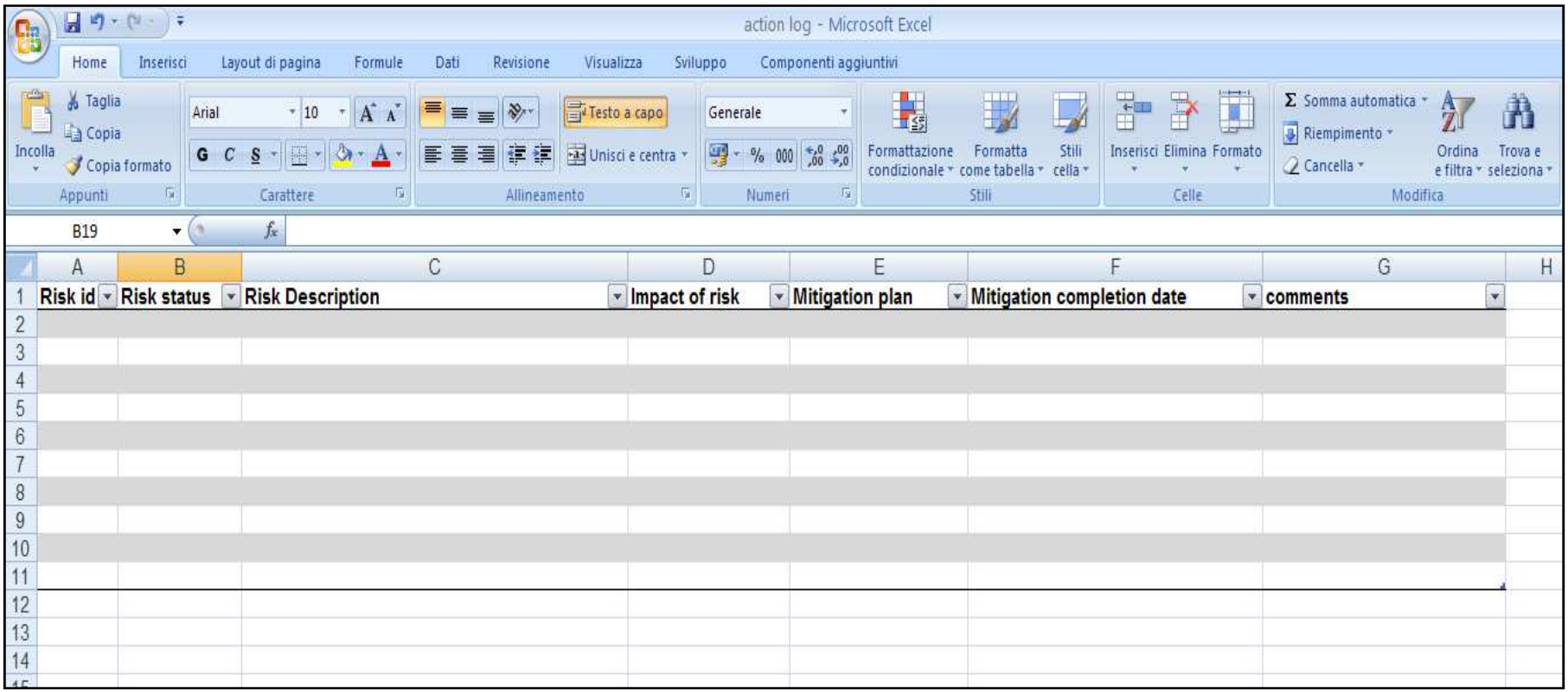
Technology Transfer

Definition and main concepts



Technology Transfer

Definition and main concepts



Risk id	Risk status	Risk Description	Impact of risk	Mitigation plan	Mitigation completion date	comments

Technology Transfer

Definition and main concepts

Knowledge management and transfer are key requirements of the TTP for preserving product quality and process performance after technology transfer.

Because of the large amount of multidisciplinary information collected, evaluated, and elaborated during the TTP, a systematic approach to acquiring, analyzing, storing, and disseminating information related to the technology should be considered and customized on the basis of the team and the project.

Technology Transfer

Definition and main concepts

- Batch records & Bill of materials
- Item specifications and justifications
- Summary of stability
- Lists of potential impurities and degradants and typical levels
- Starting materials and material safety data sheets
- Assay-related documents
- Drug master file for active pharmaceutical ingredients (APIs) and excipients
- Qualification of bioburden tests
- Solubility profiles
- Process flow diagram that provides a rationale for the synthesis, route, and form selection; technology selection; equipment;, clinical tests; and product composition
- Vendor qualification (for transfers to contract manufacturing organizations [CMOs])
- Training protocols
- Process validation report and master plan & Cleaning validation protocols and reports
- Project implementation plan & Risk assessments performed for the process or testing.

Technology Transfer

Definition and main concepts

Technology Transfer Protocol

A roadmap must be designed from the very beginning of the project to ensure comprehensive project management. The SU and RU should jointly develop a TTP plan that will govern the entire project. Critical inputs to the technology transfer plan include a regulatory strategy and a gap analysis

Outputs of this stage include a finalized project plan describing activities, resources, schedule, and project risk assessment.

Technology Transfer

Definition and main concepts

The Technology Transfer Protocol document should drive the overall process and define the strategic approach by describing at least:

- The manufacturing process being transferred
- Sampling and testing steps
- Roles and responsibilities of the SU and the RU
- RU's equipment and facilities
- A brief description of both sites (SU and RU) that includes gaps and/or differences
- Documentation requirements
- Project schedule, including roles and responsibilities of personnel (a Gantt chart is helpful here)
- Technology transfer tools, including templates
- Risk list and mitigation plan
- Correlations to previous and subsequent tasks

Technology Transfer

Definition and main concepts

- The technology transfer protocol must establish the context for the TTP, including internal and external contextual factors and which risk-management tools to use. The external context might include competitive, financial, regulatory, legal, environmental, and cultural aspects. The internal context can involve company policies and procedures, systems, operational objectives, personnel training and knowledge, available resources, and culture.
- All personnel with management roles in the transfer, including the two team leaders, should agree to and sign the project plan. A gate review by senior leadership (or sponsor) is used to make visible the plans and risks and provides approval to move to the next stage. In same cases project committee, which has a mainly consultant role, could be useful for the success of the project.

Technology Transfer

Definition and main concepts

Technology Transfer Protocol involves:

- Procedure in place to handle documentation exchange, review and evaluation within unit and between S & R units
- Reviewers list and approvers list
- QA/RA overall super-visioning of the document and its contents

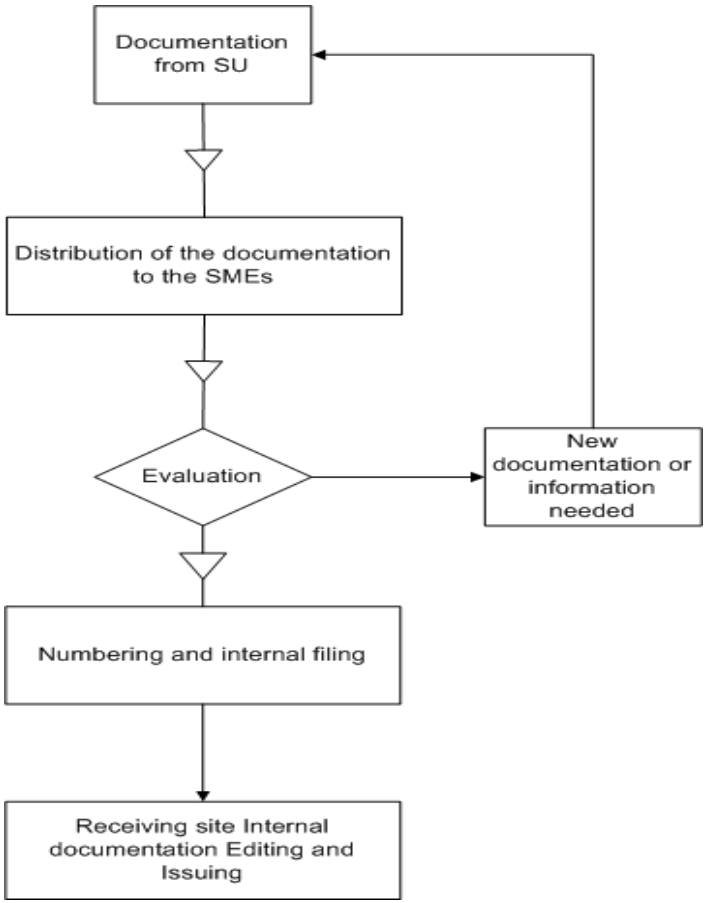
Technology Transfer
Definition and main concepts

SOP for Handling project documentation

- Chapter 1. *Application area:* Which kind of documents are needed
- Chapter 2. *Responsibilities:* Who is responsibile for what
- Chapter 3. *Documentation flow:*
  - How the documentation is received from the SU
  - How it's distributed among the team
  - How it's stored and numbered

Technology Transfer
Definition and main concepts

Visual Management support



Technology Transfer

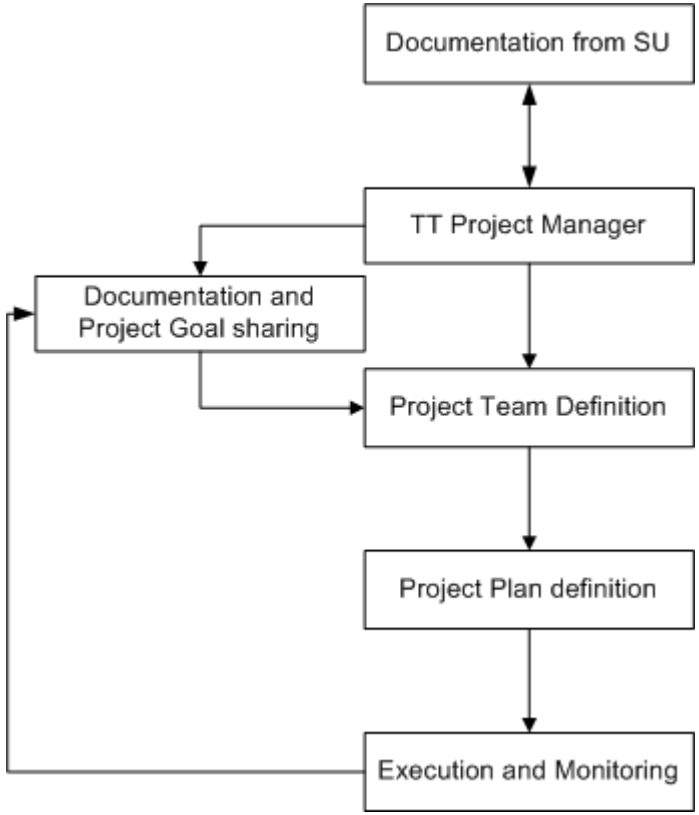
Definition and main concepts

SOP for Project Handling

- Chapter 1. *Application area:* Which kind of projects are managed
- Chapter 2. *Main roles*: Who is involved in the project
- Chapter 3. R*esponsibilities:* Who is responsibile for what
- Chapter 4. Project identification procedure (codes, numbering)
- Chapter 5. Project planning tools
- Chapter 6. Project monitoring and closure tools

Technology Transfer
Definition and main concepts

Visual Management support



Change control form

- The RU should manage the transfer via its change control procedure, and a general risk management analysis should be performed to evaluate the impact of the process on the affected departments.
- The RU should then translate the R&D information and procedures (e.g., specific activities, batch records) and adapt the process flow to fit the designated department through creation of specific procedures.
- Analysis of raw and auxiliary materials should be performed to identify and qualify suitable suppliers and materials. A risk management approach should also be applied classify and evaluate the impact of process changes aimed at optimizing the process itself.
- In the course of scale-up, process parameters and equipment may be subjected to change. Procedures should be in place at the RU to efficiently manage any changes while maintaining traceability.

Technology Transfer

Definition and main concepts

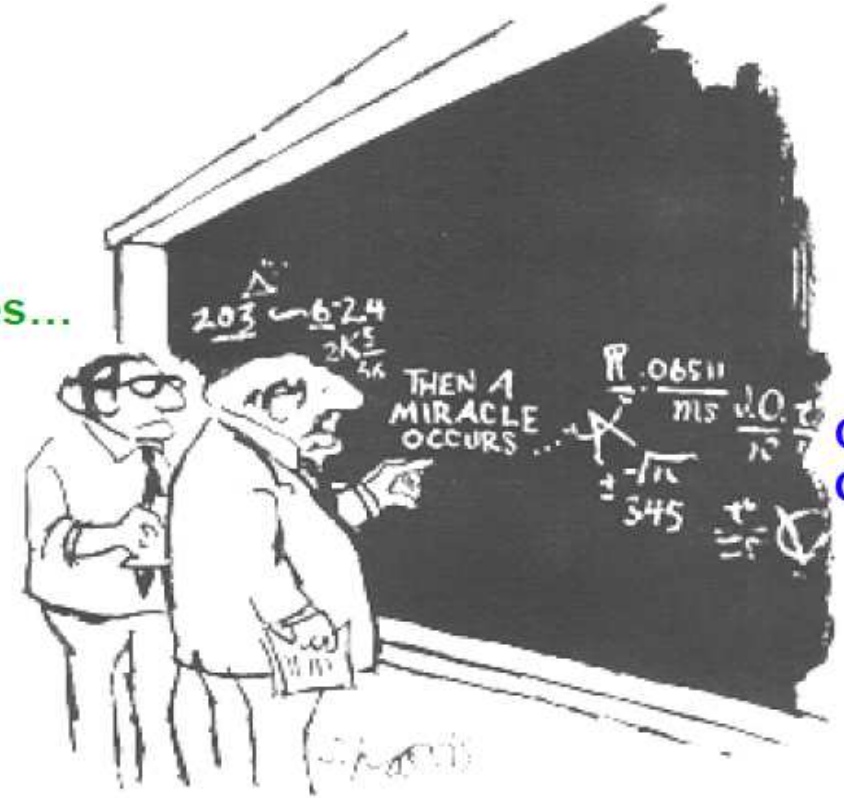
CCF should take into account any documents submitted to regulatory authorities and the possibility of their amendments.

- Filtration areas & Media
- Operating pressures and flow rates
- Process hold times
- Cleaning solutions/procedures and rinse volumes
- Devices (e.g., changing from housing to a filter-press for depth filtration)
- Disposable containers versus stainless steel (or vice versa)
- Process development reports should detail the rationale to support any changes. The application of good documentation practices and design of experiment techniques during process development are fundamental to support these changes and the application of GMPs during clinical manufacturing.
- Insertion of new steps or modification of process flow should be carefully evaluated from quality and regulatory points of view.
- In the event of a substantial process modification, the transfer should be put on hold and feasibility studies performed again.

Technology Transfer

Definition and main concepts

R&D Processes…



Commercial Operations …

"I think you need a few more details here in the Transfer protocol"

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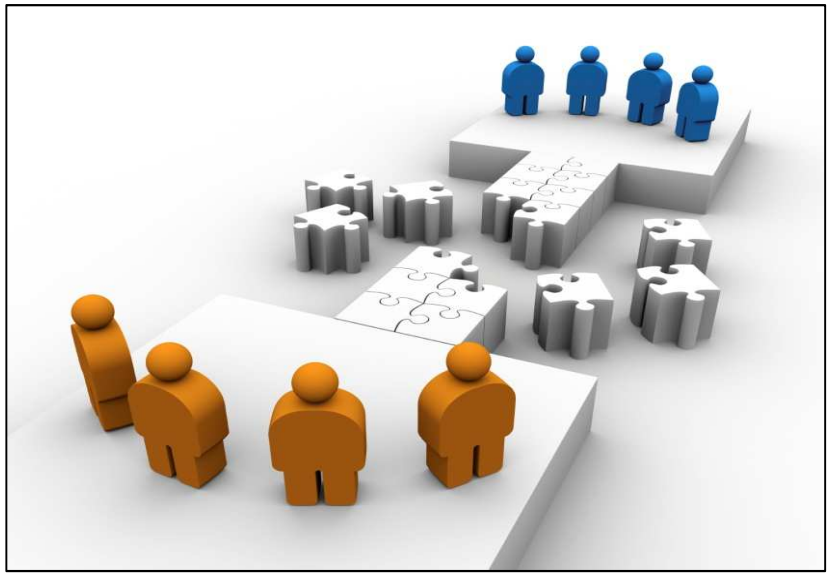
Technology Transfer

Definition and main concepts

- Technical Skills
- Planning
- Multitasking and Organization
- Flexibility
- Troubleshooting
- Negotiation
- Goal oriented



Technology Transfer

Definition and main concepts

The Tech Transfer Project Manager:

- In depth knowledge of the site (manufacturing areas and equipment, quality control, quality assurance) GMP, regulations, process flow, markets, new tools for project management. All of which are updated continuously.
- Highly Motivated and a strong sense of **ownership** and **urgency**.
- The TTPM must be a person capable to manage and influence all the functions on the site i.e. strong ability in keep control over all the aspects of a project and communication to the client/project needs with a high level of transparency. **The TT must stay in the heart of the process and manage all aspects**.
- Every decision must be challenged in the interest of the client and the project.
-**The Project Goal is at the center of our activities!** Managing the project and the product in respect of GMP rules and timelines. Keeping control of the financial and legal implications of all the activities to be delivered.

Technology Transfer
Definition and main concepts

– **TTPMs are the "*General Manager of the project*" for our clients**

– Take ownership of project/product opportunities and drive them **from early quotation stages to <u>manufacturing and routine supply</u>:**

- Relationship management – **Key window for the sending unit into the receiving unit**
- Relationship management – **Key and entrusted** by all the members of the TT team
- Project / Opportunity **Cost Evaluation and Budget management**
- Contract Negotiation and ongoing MSA maintenance
- **Project Management – leading all company functions, Operations, Quality, Finance, Quotation group, Business development and Account executives.**
- Financial Reporting – revenue forecasting

The TTPMs have a strong site technical knowledge linked with business acumen

……is all about leading without authority to create collaboration among component teams by managing at interfaces to maximize program benefits realization• Skills are far more important than any process

Technology Transfer Project

Project Management (PMBOK)

- "A project is a temporary endeavor undertaken to create a unique product, service, or result"
- Project Management is: "The application of knowledge, skills, tools, and techniques to project activities to meet the project requirements"

PMBOK Project Stages

- Initiation
- Planning
- Execution and Control
- Close Out

Technology Transfer Project

- Deliverables: licensed manufacturing of a robust process
- Timeline: from siting decision to license approval and commercial manufacturing
- Application of Project Management tools

Project Plan

Project Plan Components

- **Responsibilities**
- **Resources**
- **Duration**
- **Status monitoring**
- **Tasks**
- **Governance plan**
- **Strategies – Regulatory, Process Qualification, Manufacturing**

Technology Transfer

Definition and main concepts

Data Analysis

Realization

Implementation

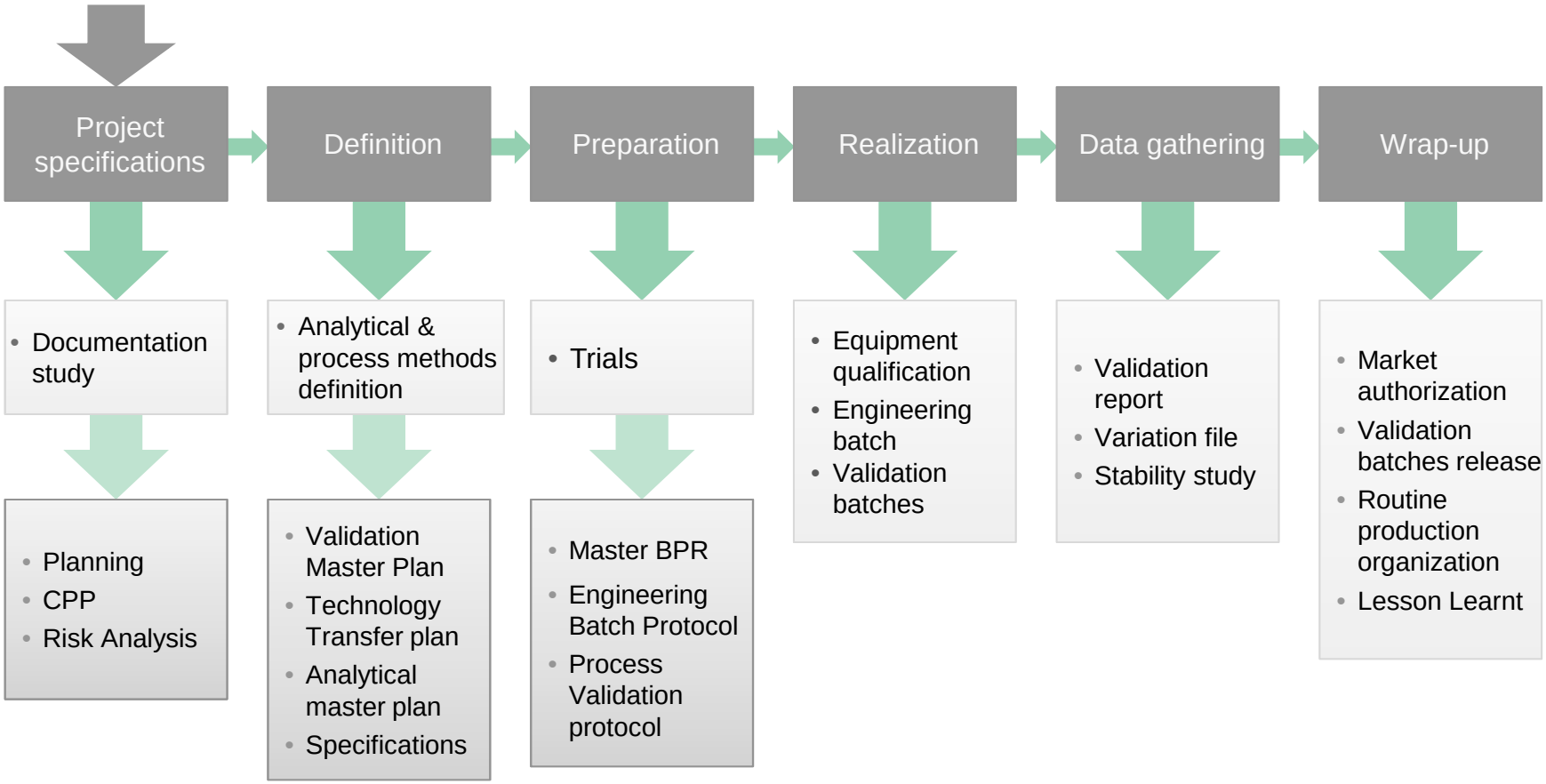
Definition

Assessment

Technology Transfer

Definition and main concepts

- Regulatory file
- Technical data
- EHS data



Quality Risk Management

B5

Some Useful Terminology

- **Risk**

  - combination of the probability of occurrence of harm and the severity of that harm

- **Quality Risk Management**

  - Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the drug product across the product lifecycle.

- **Risk reduction**

  - processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level.

- **Risk acceptance**

  - formal decision to accept the residual risk or a passive decision in which residual risks are not specified

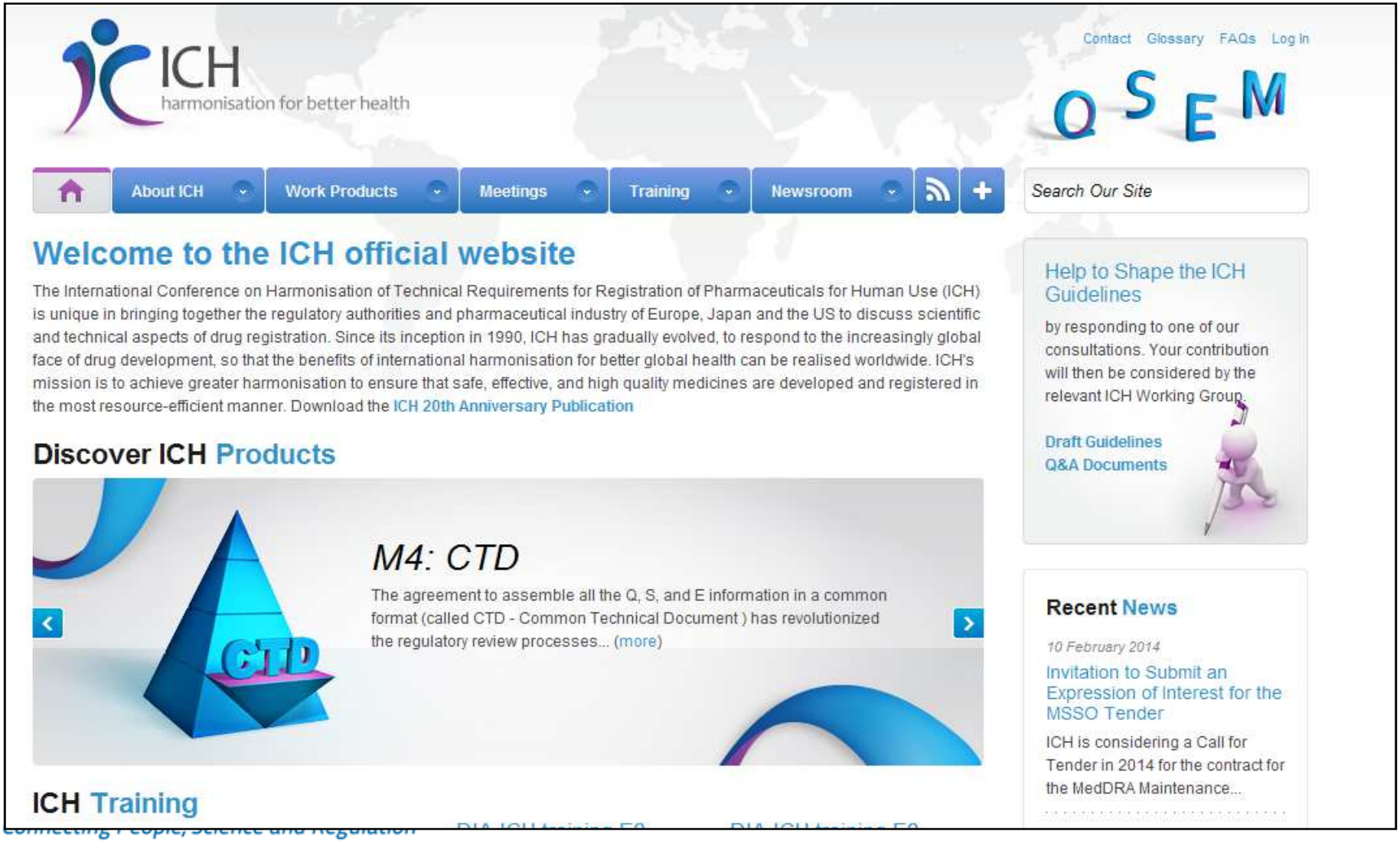
- **Risk communication**

  - sharing of information about risk and risk management between the decision makers and others

Diapositiva 68

B5 Suggestion of a defition slide:
but please modifie the definition as needed
Backes; 13/06/2014

ICH & Risk - http://www.ich.org/



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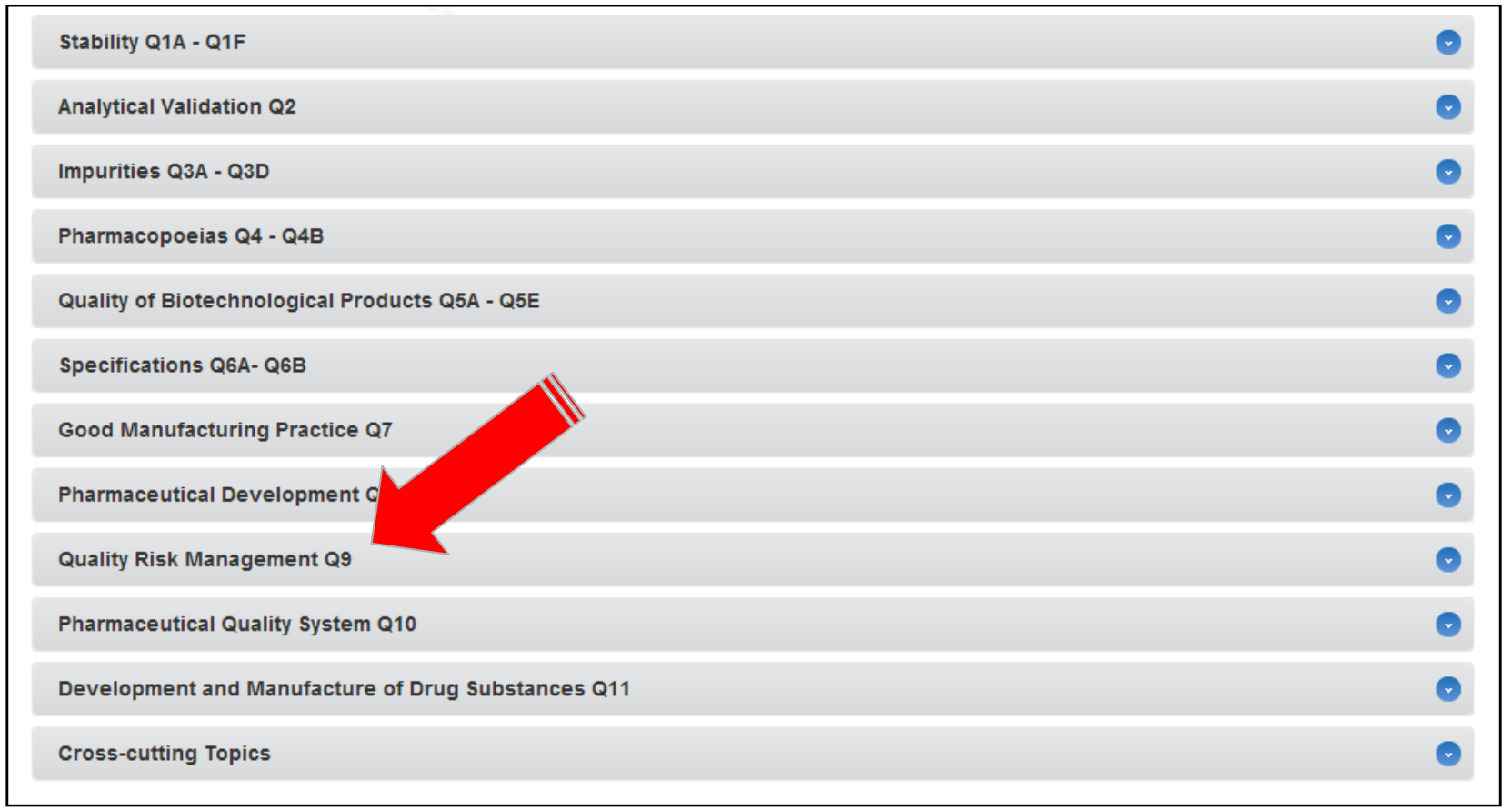

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- It is commonly understood that risk is defined as the combination of the probability of occurrence of harm and the severity of that harm.

- In relation to pharmaceuticals, although there are a variety of stakeholders, including medical practitioners as well as government and industry, the protection of the patient by managing the risk to quality should be considered of prime importance.

- It is important to understand that product quality should be maintained throughout the product lifecycle such that the attributes that are important to the quality of the drug (medicinal) product remain consistent with those used in the clinical studies.

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Two primary principles of quality risk management are:

• The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient;

• 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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Quality risk management activities are usually, but not always, undertaken by interdisciplinary teams. When teams are formed, they should include experts from the appropriate areas (e.g., quality unit, business development, engineering, regulatory affairs, production operations, sales and marketing, legal, statistics, and clinical) in addition to individuals who are knowledgeable about the quality risk management process.

Decision makers should

• take responsibility for coordinating quality risk management across various functions and departments of their organization and

• ensure that a quality risk management

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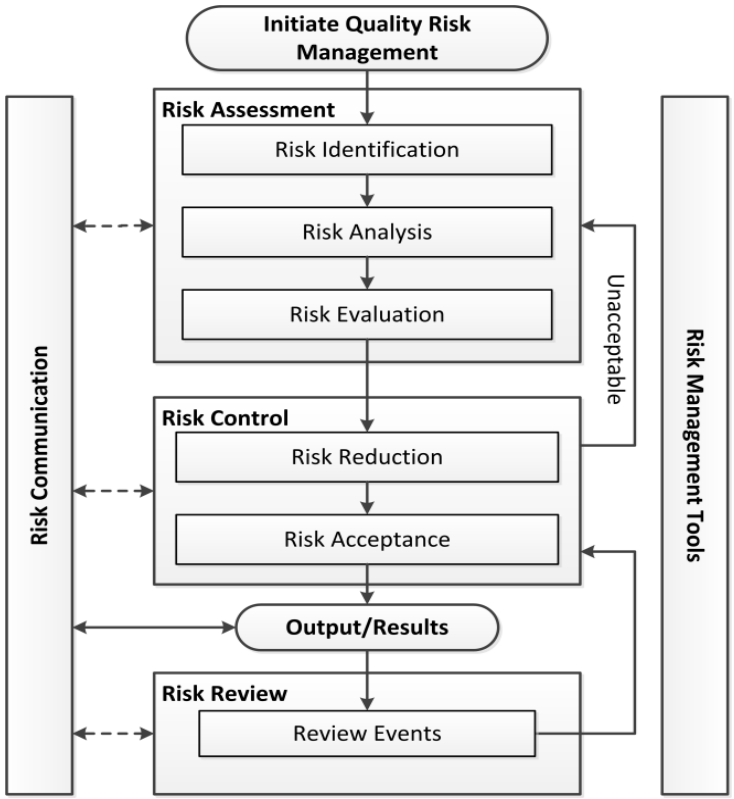
The quality risk management (QRM) is “a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle.”



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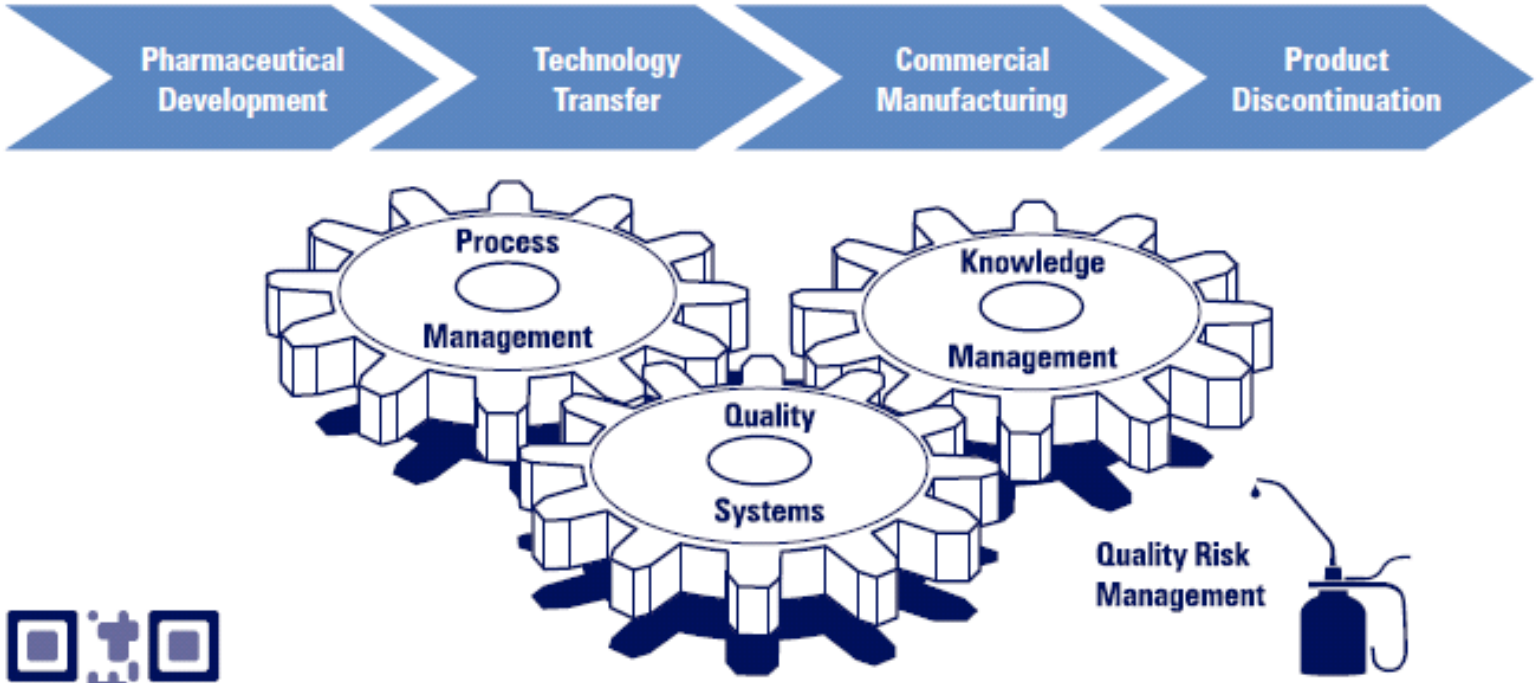
ICH Q9

ICH & Risk – PMCO Program

The Product Life Cycle



For more information, including the PCMO Dossier, and to get involved, go to www.pda.org/pcmo

ICH & Risk – PMCO Program

Risks of Technology Transfer

- Often, poor attention to its objectives (e.g., too tight or too broad process specifications) destines a TTP for failure. Technology transfer can affect drugs and patients. Consequently, in all technology transfer activities that a project team designs and executes, the team needs to keep in mind the scope of the technology being managed and the potential impact of technology transfer failure.

- Some common risks are:
  - Lack of information
  - Objective that is not clear (or clearly defined) or not properly communicated and/or shared
  - Poor preliminary assessment with lack of changes identification
  - No or poor assessment of the effects of changes to the objective
  - Lack of project management

ICH & Risk - http://www.ich.org/

As applied to Technology Transfer (TT), QRM can be useful to cover the risks involved in the process being transferred from the sending unit (SU) to the receiving unit (RU) as they relate to the maintenance of product quality attributes

Some risk management tools mentioned in ICH Q9 applicable to TT are:

- Basic risk management facilitation methods (flowcharts, check sheets, etc.)
- Failure Mode Effects Analysis (FMEA)
- Failure Mode Effects and Criticality Analysis (FMECA)
- Fault Tree Analysis (FTA)
- Risk ranking and filtering
- Supporting statistical tools

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Stage Gate	Strategy	Analytical and Quality Control Testing	Regulatory	Process	Facilities/ Engineering	Risk Management and Components
1 Planning	Perform preliminary risk assessment prior to beginning late-phase development using risk ranking and/or preliminary hazards analysis approach.					
2 Process Readiness	Update preliminary risk assessment (transition to PHA)	Update risk assessment (transition to PHA) for SU and RU readiness for AMT	Risk mitigation through SLA and quality agreement between SU and RU	Update risk assessment (transition to PHA) for manufacturability of late-phase development process	Update risk assessment (transition to HAZOP) for operating process at manufacturing site	Update risk assessment (transition to PHA) for RMs/ components, including assessment of the impact of any changes in the suppliers or manufacturing sites of the RMs
3 TTP implementation and Qualification	Review and update risk assessment/PHA from stage gate 2 if necessary. Mitigate identified high risks.					
4 Licensure & Manufacturing	Convert PHA risk assessment from stage gate 3 to FMEA/FMECA risk assessment, including re-evaluation of risk ranking after risk mitigation plan implementation					
	Update risk assessment from stage gate 4 for commercial process	Complete risk assessment for SU and RU readiness for AMT	Risk mitigation through SLA and quality agreement between SU and RU	Update risk assessment for manufacturability of commercial process	Update risk assessment (HAZOP) for operating process at commercial site	Update risk assessment for RMs/components, including assessment of the impact of any changes in the suppliers or manufacturing sites of the RMs

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- The selection of a risk management approach should be done at the beginning and applied along the TTP. This approach will facilitate decision-making at different points throughout the TTP while ensuring that all activities are performed in a manner that protects patient safety.

- To realize the utmost benefit from QRM, companies must adapt their culture, systems, and procedures. They must shift from a risk-averse to a risk-aware culture by creating procedures and tools that enable individuals to apply benefits from QRM to the TTP

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As applied to Technology Transfer (TT), this activity, done at the beginning of the project, can detect the most likely potential causes of technical failures and allow planning for mitigating those risks.

Following ICH Q9, the risk can be estimated based a combination of three main factors:

- Severity (S)
- Occurrence (O)
- Detection (D)

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Severity considers the potential impact on the quality attributes of the product and hence on patient health.

It can be rate based on the table below

Severity	Risk Classification	Value
No impact on the product's quality attributes or on patient health	Negligible	1
Moderate impact on product's quality attributes and on patient health	Moderate	2
Severe impact on product's quality attributes and on patient health	Critical	3

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The occurrence factor is defined as the frequency of occurrence of the event. In a TTP phase, occurrence is based on the combination of the SU knowledge of the product and the RU experience on process.

It can be rate based on the table below

Occurence	Risk Classification	Value
Highly improbable or impossible that the negative event occur	Remote	1
Some possibility that the negative event will occur	Medium	2
Highly probable or certain that the negative event will occur	High	3

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The detection factor is defined as the probability of detecting the events if they occur, based on the control system in place.

It can be rate based on the table below

Probability	Risk Classification	Value
Highly probable or certain that the negative event will be detected by the control system in place	Remote	1
Some possibility that the negative event will be not detected by the control system in place	Medium	2
Highly improbable or impossible that the negative event will be detected by the control system in place	High	3

Product/process regulatory assessment: - Assess and Plan since the beginning

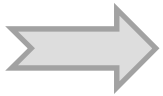
- Submission file review:
  - Is the dossier available?
  - Is the approval letter from the market countries available? Is the approval still pending?
  - Which procedures has been used for the submission?
  - Are review processes ongoing for the product?
  - Does a gap analysis between current submission and current process exist?

- Process specific review:
  - Is there any BS change? If yes, is it within the 10x?
  - Is there any CPP change?
  - Is there any IPC/FP/incoming change?
  - Is there any equipment change?
  - Is there any process step change?

Technology Transfer
Regulatory Compliance

Product/Process regulatory assessment:

- Analytical assessment:
  - API/raw materials:
    - Which is the origin of the API and RM? *(EU, non EU, RoW)*
    - Are those compliant with GMP/ICHQ7A? *(QP declaration on FP)*
    - Does API has a DMF, CEP?
    - Are all the certification available? (TSE/BSE, Residual solvents, genotoxic impurities, metal catalyis components)
    - Which are the storage conditions, retest conditions, expiry date?
  - FP:
    - Which is the status of the analytical methods? *Fully validated, assessed, etc*
    - As a part of the transfer project are we going to change the analytical plan?
    - As a part of the transfer project are we going to change the limit ranges?
    - As a part of the transfer project are we going to change the stability specs or the storage/shipment conditions?
- Primary packaging
  - As a part of the transfer project are we going to change the primary packaging components?
  - Which are the tests on those primary packaging components?



Assess and plan before start!

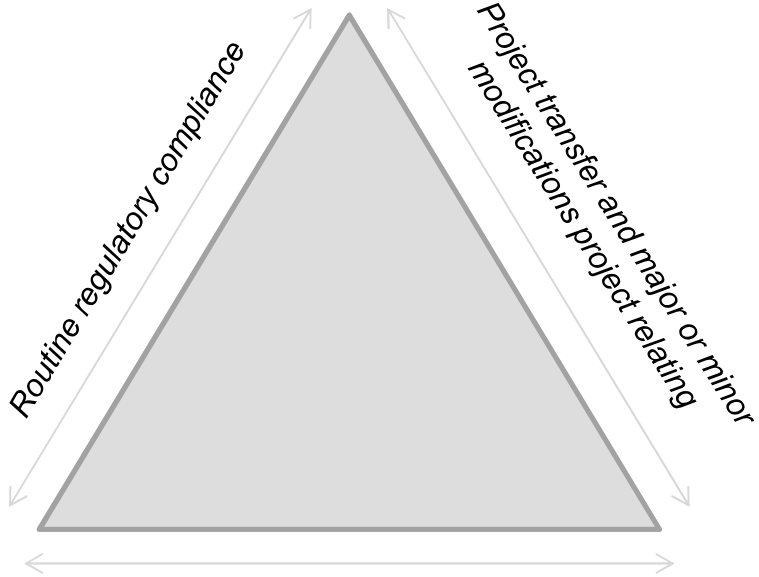
Technology Transfer
Regulatory Compliance

- Gap Analysis / Summary Form
  - Issuing of a formal Gap analysis in which RA requirements and RA strategy are detailed. Data to be generated during transfer have to be highlighted as well.
- Project execution
  - Always include RA input on the technical documentation issued along the project (i.e Process validation and equipment validation documents, specifications, MBR, Analytical methods)
- Project end
  - Based on Regulatory strategy and market destination requirements, edit and circulate among the project team the submission file.

Technology Transfer
Regulatory Compliance

"Triangle Approach"

Sending unit (B)
(manufacturing / Analytical service / PCK)



Marketing Authorization Owner (A)
(market authorization and product dossier)

Receiving Unit (B')
(manufacturing / Analytical service / PCK/Releasing)

Technology Transfer

Definition and main concepts

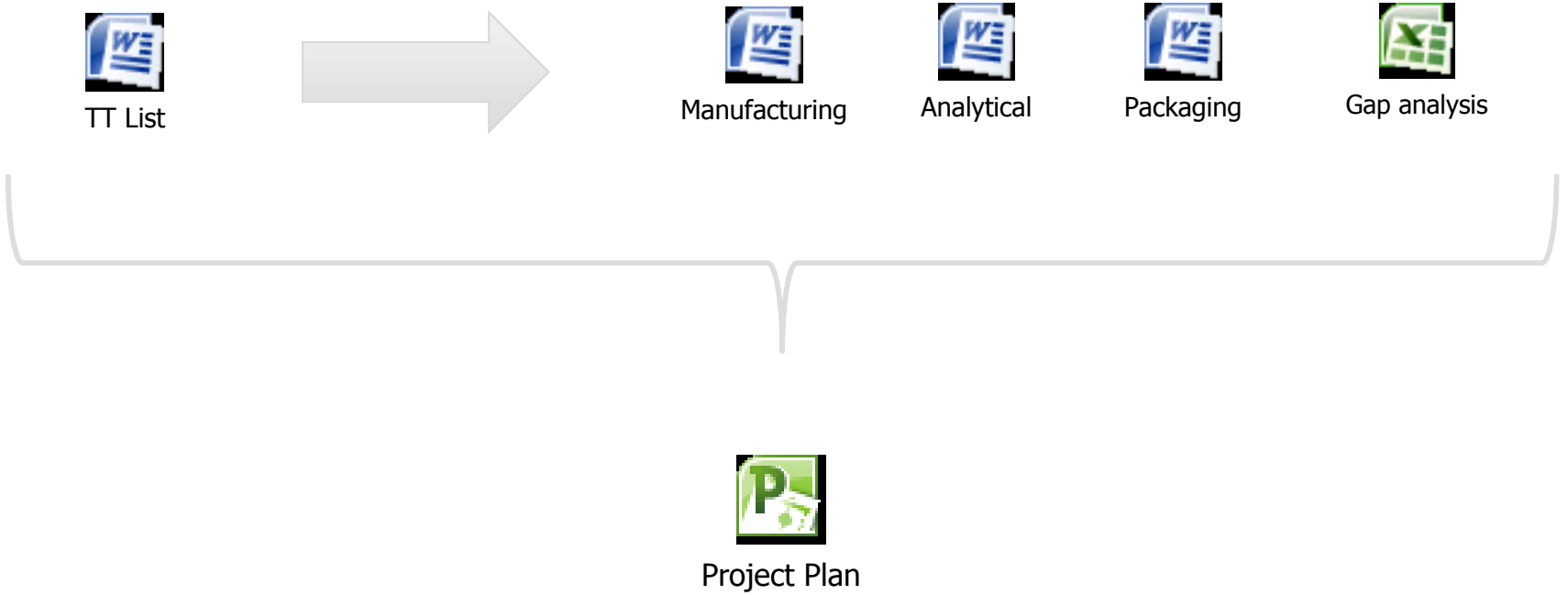
Case Studies experience

Template tools used in

Assessing, Planning, Execute & Monitoring

Technology Transfer

Definition and main concepts



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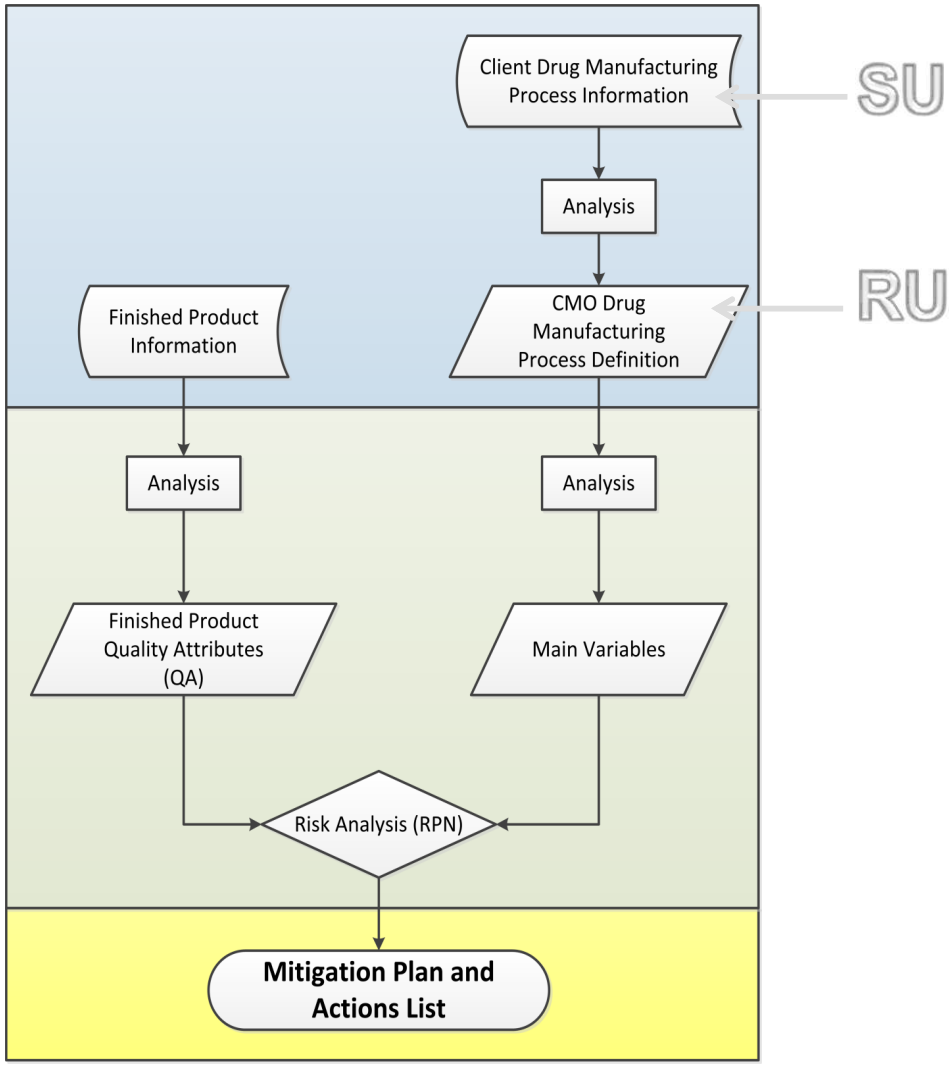

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STEP 1 – Definition of the Quality Attributes of the product (SU -> RU)

List of main items considered for the evaluation	Relative Variables		
Process	Mixing Holding Compounding Grade C filtration Grade A filtration	Filling Stoppering Crimping Solution transfer Steam terminal sterilization	Identification Wrapping Visual inspection Secondary packaging Line cleaning
Primary packaging and GMP materials	Stoppers Vials Seals	Filters Disposable tubes Disposable bag	Fixed tube Gasket
API and excipient attributes	API pH API appearance	API density API osmolality	Excipient attributes

STEP 2 – Definition of the Process Variable (RU)

Quality Attribute		
Appearance	pH	Volume in container
Identity	Density 20°C	Cosmetic appearance
Assay	Osmolality	Sterility
Impurity	Particle matter	Endotoxins

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Process	Mixing, Compounding	pH	Dissolution time insufficient for complete dissolution and an homogenous system	3	3	1	9	During the Performance Qualification, the mixing device of the tank used in the RU will be challenged.
		Osmolality	Dissolution speed insufficient for complete dissolution and an homogenous system	3	3	1	9	Mixing studies will be agreed with the SU and performed during the engineering batch.
		Appearance	Mixing system not appropriate to guarantee uniform batch mixing	3	3	3	27	The User Requirements of the RU tank have properly defined the mixing needs based on the characteristics of the colloidal system. The initial evaluation and information sharing between SU, RU and the disposable technology Supplier have identified the appropriate mixing device. The PQ challenge of the mixing system will include appropriate tests suggested by the supplier/owner of the technology
		Density	Temperature of the system out of range specified by the SU	2	1	1	2	*No further action needed.* The colloidal system is not sensitive to temperature. The RU WFI loop cooling and temperature control system will guarantee a 15-25°C range.
			Sampling mode device impact on the analysis results	3	2	2	12	The sampling system will be made of pharmaceutical grade glass. The SU have collected data on compatibility and the solution is declared compatible with glass devices.
		Sterility	Preparation time impact on bioburden level of the final compounded solution	3	2	2	12	Validation activities will include hold time challenges according to a dedicated protocol. Chemical characteristics and microbiological attributes of the solution will be analyzed.
		Particulate matter	Particle release from disposable hoses may impact the particulate matter profile	3	2	3	18	Use Silicon, Pt-cured, disposable hose certified for pharmaceutical use for solution transfer. To address particle release from the hoses used in Grade C, filter the solution 3 times before filling (0.45 um + 0.22/0.2 um in grade C area and 0.22/0.2 um in grade A area). Regarding the particle release from the hoses used on the filling machine, a final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Process	Mixing, Compounding	Particle Matter	Mixing system shedding may impact the particulate matter profile	3	2	3	18	Supplier has provided leachable/ extractable documentation and certifications. Compatibility studies to be conducted with specified analytical methods with the supplier.
	Grade C and Grade A Filtration	Particle Matter	Release from the filter membrane may impact the particle matter profile of the solution	3	2	3	18	Regarding the release from the filters used in Grade C, the solution is sterile filtered before filling. A final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.
		Sterility	Filter with integrity issue can compromise the sterility of the solution	3	1	1	3	The filter arrives in the RU with the integrity certification of the supplier. According to the RU procedure, each 0.22/0.2 um filter is tested after and before use. Leachable/extractable documentation and certifications will be provided by the supplier. If needed, specific analyses can be done by the supplier to identify possible leachables and extractables. Adsorption and compatibility studies will be performed as a part of the filter validation.
			Filter clogging	3	1	1	3	Clogging of the filter with potential impact on the sterility of the overall process is evaluated in a preliminary phase of the transfer, including supplier trial for scale up of their size. Analysis of the exact filtration system and critical process parameters that will be used during drug manufacturing are necessary. Both Velocity max or Pressure max trials are reliable and can anticipate potential failures. Media fill challenge of the filter change procedure is a valid practice to downgrade the associated risk and estimate the impact on sterility as a result of the filter change.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Process	Grade C and Grade A Filtration	pH	Adsorption on the membrane filter can impact density, osmolality and pH of the solution	3	3	3	27	Adsorption studies will be done as a part of the filter validation. High impact has to be considered in the case of biological compounds due to potential impact of changes in preservative concentrations.
		Density	Incompatibility between filter and solution can modify the system chemical profile	3	3	3	27	Compatibility studies will be done as a part of the filter validation
		Sterility	Clogging issue can have impact on the microbiological growth attributes and chemical characteristics of the solution	3	3	2	18	The appropriate size of the filter will be defined in the RU with a specific lab trial with the filter supplier. The solution will be filtered through the filter until clogging occurs. Volume filtered, time of filtration, surface area, and flow rate will be analyzed and correlated. The RU minimum filter size will be defined. A dedicated protocol and report will be issued with the results of the trial.
		Sterility	Holding time before filtration can increase the bioburden of the compounded solution	3	2	2	12	During the validation activities, the holding times will be challenged according to a dedicated protocol. The chemical characteristics and microbiological growth attributes of the solution will be analyzed.
	Filling	Volume in container	Incorrect filling weight can result in out of range container volume	3	1	1	3	No further actions needed because the RU procedures are already in place to periodically check the weight of the solution dosed into the vials during filling activities.
		Particle matter	Particle release from the tube can impact the particle matter profile of the solution	3	2	3	18	Certified Silicon, Pt cured, disposable hose for pharmaceutical uses will be chosen for the solution transfer. A final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.
	Stoppering	Sterility	Incorrect positioning of the stopper on the vials can result in incorrectly closed containers	3	1	1	3	An appropriate sensor device is in place in the RU to check the correctness of the position of the stopper on the vials before the crimping step.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Process	Crimping	Cosmetic Appearance	Incorrect sealing of the vials can result in cosmetic defects	2	1	1	2	No further actions needed because according to the RU standard approach, a validation of the crimping will be done. The validation will take into consideration the cosmetic appearance of the vials. Moreover according to the RU procedure, the cosmetic appearance of the crimped vials is periodically checked during the batch.
		Sterility	Incorrect sealing of the vials can result in a non-closure of the vials	3	3	3	27	Validation of the crimping step will be done. During validation, the correctness of the crimping will be challenged from a cosmetic point of view and from a container closure point of view by dye intrusion test. Vials will be analyzed by UV-Vis after immersion in a solution of methylene blue.
	Steam terminal Sterilization	Sterility	Assurance of an appropriate sterility cycle has to be guaranteed to provide the required lethality	3	3	2	18	The terminal steam sterilization cycle will be validated to guarantee sterility assurance
		pH	pH shift due to thermal stress can modify the chemical characteristics and consequently the stability of the solution after the TS	3	3	1	9	A technical report on the previous lots manufactured will be shared between Receiving and SU. The pH shift will be calculated. Based on the report, an appropriate pH range prior to terminal sterilization will be set. An in-process control and an appropriate pH adjustment step prior to terminal sterilization will be introduced in the batch record to guarantee the correct pH of the final sterilized solution. The validation batches manufactured in the RU will undergo a stability study to confirm that no changes of the system profile occur.
		Appearance	Flocculation, Coagulation events due to thermal exposure may impact the use and the stability of the solution	3	3	1	9	Appearance is one of the tests performed on the solution at the end of the process after the terminal sterilization.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Process	Identification	Cosmetic Appearance	The incorrect setting of the laser printer used for the identification of the vials could impact vial identification	3	1	1	3	No further action needed, the RU procedure already in place guarantees the correctness of the setting of the laser print. Moreover during the production activities the accuracy of the vial identification label is checked periodically.
	Wrapping (Bulk Pkg.)							
	Visual Inspection	Cosmetic Appearance	A defects checklist that has not been properly reviewed can lead to vials sent to the SU not matching SU expectation	3	1	1	3	A checklist dedicated to the products will be generated based on RU experience and SU requirements. The checklist will be reviewed and approved by the SU as well. Appropriate training will be conducted for the Visual Inspection Department operators.
	Secondary Packaging							
	Line Cleaning	Density Osmolality Impurity	Possible residual material from the previous batch may be transferred to the following batch and could modify the chemical profile of the solution	2	3	2	12	Specific cleaning validation activities will be done to validate the cleaning procedure to be applied after each batch manufactured.
			An incorrect ARL can lead to false evaluation of the cleanliness status of the line	3	1	2	6	As a part of the cleaning validation, appropriate calculation will be done to define the ARL based on current guidelines. All cleaning validation activities will be detailed in dedicated protocols and reports reviewed and approved by the SU.
			Inappropriate analytical method can lead to false results	3	1	2	6	A specific method to analyze the WFI at the end of the cleaning procedure will be developed and validated to guarantee the accuracy and reproducibility of the results obtained.
			Cross-contamination with other products can compromise the quality of the solution	3	2	3	18	All lines and machine parts in contact with the product will be dedicated to avoid cross contamination.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Primary Packaging & GMP materials	Stoppers	Impurity	An impurity from the stopper can modify the solution chemical profile	3	2	3	18	The stopper components have been chosen by the SU during the development studies.
			The coating material can modify the chemical solution profile	3	2	3	18	The same stoppers will be used to guarantee no anomalous interaction with stopper coating and rubber.
		Appearance	Substances released from the stopper or from the coating can induce flocculation or coagulation events in the solution	3	2	1	6	Stability data were collected by the SU; no interaction issues were reported to RU.
			Substances released from the stopper or from the coating can modify the appearance of the solution	3	2	1	6	
		Sterility	The bioburden of the stopper can impact the effectiveness of currently used and validated sterility cycles	3	1	3	9	A risk assessment will be done to compare the several stoppers currently used in RU with the SU stoppers, to evaluate the possibility to use a sterilization cycle already validated. In the case in which no comparable stoppers are found, a new stopper sterilization cycle will be validated.
		Particle Matter	Release from the stopper may impact the particle matter profile of the solution	3	2	3	18	A final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.
	Vials	Impurity	Impurities released from the glass can impact the solution profile	3	2	3	18	Type I glass, USP/EP grade will be used. The validation batches produced will be analyzed via stability study. All release tests will be repeated regularly during the stability program to confirm no anomalous changes to the system profile.
			Leachables and extractables from the glass can modify the chemical profile of the solution	3	2	3	18	
		Appearance	Leachables, extractables, and ions can induce flocculation or coagulation of the system	3	2	1	6	
		Cosmetic Appearance	Vials of finished product can be rejected for cosmetic defects	2	2	1	4	*No further actions are needed.* Incoming statistical checks will be done on each lot of vials prior to use. An agreement with the supplier is in place that defines appropriate AQLs for each defect. These AQLs are in line with the cosmetic requirements received by the SU.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Primary Packaging & GMP materials	Vials	Endotoxins	An incorrect depyrogenation cycle can impact the endotoxin level of the final product	3	1	3	9	Validation activities will be done on the tunnel to determine an appropriate depyrogenation cycle. A maintenance program is in place for all the equipment used in production. The raw data of each vial depyrogenation cycle must be attached to the executed BR.
		Particle Matter	Material released from the glass can modify the particle matter profile of the final product	3	1	1	3	Type I glass, USP/EP grade will be used. A validated cycle will be applied to wash the vials before the depyrogenation step. A final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.
	Seals	Cosmetic Appearance	Damaged seals can impact the crimping step and/or lead to rejected vials	2	2	1	4	No further actions are needed. Incoming statistical checks will be done on each lot of seals prior to use.
	Filters	see filtration step of the Process section						
	Plastic Disposable Bag for solution preparation	Density Osmolality pH	Impurities from the product contact layer can modify solution chemical characteristics	3	3	3	27	Leachables/extractables documentation and certifications will be provided by the supplier. In case of further necessity, specific analyses can be done by the supplier to identify possible leachables and extractables. Compatibility studies will be done together with the supplier with specific analytical methods. Appropriate IPC controls of pH, density, osmolality and appearance, are established to check the correctness of the prepared solution attributes. A final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.
		Appearance	Release from the product contact layer of the bag can generate flocculation or coagulation events	3	3	1	9	
		Impurity	Leachable and extractable from the product contact layer can modify the chemical profile of the solution	3	3	3	27	
		Particle matter	Release from the product contact layer of the bag can modify the particulate matter profile of the final product	3	1	1	3	
	Disposable Tubes	see filtration compounding and filling step of the Process section						

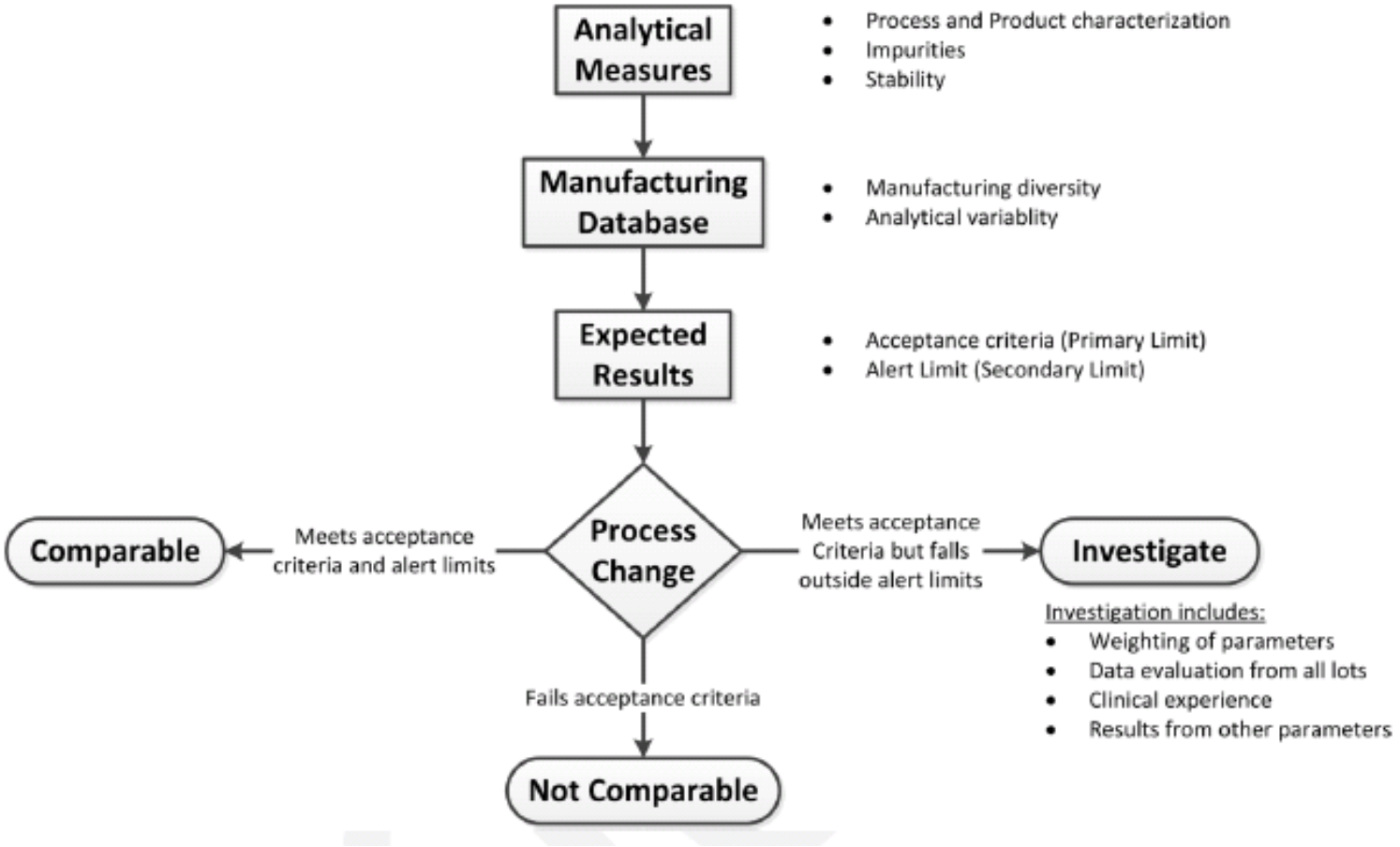
ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
Primary Packaging & GMP materials	Fixed Transfer line and Contact Parts of the filling machine	Density Osmolality pH	Adsorption to the lines or contact parts can impact the chemical profile of the solution	3	2	2	12	The chemical and microbiological characteristics of the solution prepared will be analyzed prior to filling and a complete set of analyses will be done at the end of the manufacturing for release of the lots.
			Incompatibility issue can modify the chemical profile of the solution	3	2	2	12	The compatibility of the system with all the materials used along the process will be confirmed with the SU. If there is no data available or in case of doubt, appropriate compatibility studies can be agreed with the SU and performed in RU.
		Sterility	Inappropriate sterilization procedure can negatively impact the sterility assurance of the process	3	1	3	9	A Validation of the SIP Cycle will be done. Dedicated procedures will be issued to manage the sterilization of the line. All the raw data of the temperature profile during sterilization will be attached to the executed BR for each batch. A bioburden analysis of the solution at the end of the preparation and prior to terminal sterilization will be established as IPCs.
Primary Packaging & GMP materials	Gasket (PTFE, Silicon)	Density Osmolality Impurity	Adsorption to the lines can impact the chemical profile of the solution	3	2	2	12	The chemical and microbiological characteristics of the solution prepared will be analyzed prior to filling and a complete set of analyses will be done at the end of the manufacturing for release of the lots.
			Incompatibility issue can modify the chemical profile of the solution	3	2	2	12	The compatibility of the system with all the materials used along the process will be confirmed with the SU. If there is no data available or in case of doubt, appropriate compatibility studies can be agreed with the SU.
		Particle Matter	Material released from the gasket material can modify the particle matter profile of the solution	3	1	1	3	*No further actions are needed.* Regarding the release from the gaskets used in the solution preparation Grade C area, the solution is filtered 0.22/0.2 um before the acquasant (or surge tank) of the filling machine. Moreover a final 100% visual inspection will be done. Vials with a particle matter defect will be rejected.

ICH & Risk – PMCO Program

Analysis				Risk Priority Number Evaluation				Mitigation Plan
Item	Variable	QA Impacted	Potential criticality/cause of lack of quality attribute description	Severity	Occurrence	Detection	RPN	Consideration/Action
API Attributes	API Appearance	Appearance	Anomalous appearance of the API can modify solution appearance	3	1	1	3	An internal API specification will be issued with well-defined range for each test. Each lot will be analyzed and released prior to its use in production.
	API particle matter	Particle Matter	Insoluble matter in the API can impact the solution particle matter level	3	1	2	6	
	API density, pH, and osmolality	pH Density Osmolality	Anomalous pH, density or osmolality can impact the chemical characteristics of the solution	3	1	1	3	
	API bioburden	Sterility	High bioburden of the API can impact the overall bioburden prefiltration of the compounded solution	3	1	2	6	
	Excipients attributes	pH Density Osmolality Appearance Particle Matter Sterility	Each excipient characteristic can impact final product quality the	1	2	2	4	Internal specifications will be issued with well-defined ranges for each excipient test. Each lot of each excipient will be analyzed and released prior to its use in production.

ICH & Risk – PMCO Program



Technology Transfer
Day 2

Workshop 1

Technology Transfer
Day 2

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

❑**Questions**

- ❑Which Criteria will you use to select a partner?
- ❑Describe the main attribute you will suggest to look for…

Workshop 2

Technology Transfer
Day 2

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

The partner has been identified and selected.

❑**Questions**

❑Describe the main milestones to bring the product from the SU to the RU

Workshop 3

Technology Transfer
Day 2

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

The partner has been identified and selected.

❑**Questions**

- ❑Group 1. SU Describe the project team member mainly impacted in each milestone
- ❑Group 2. RU Describe the project team member mainly impacted in each milestone

Workshop 4

Technology Transfer
Day 2

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

The partner has been identified and selected. Agreement is in place, team members identified

❑**Questions**

- ❑Group 1. SU. Define the list of information/document you would prepare for the transfer
- ❑Group 2. RU. Define the list of information/document you would request for the transfer

Workshop 5

Technology Transfer
Day 2

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

The partner has been identified and selected. Agreement is in place and path defined.

❑**Questions**

- ❑Group 1. SU. Define timelines for the main milestones of the project
- ❑Group 2. RU. Define timelines for the main milestones of the project

Workshop 7

Technology Transfer
Day 2

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

The partner has been identified and selected. Agreement is in place and path defined; timelines are defined.

❑**Questions**

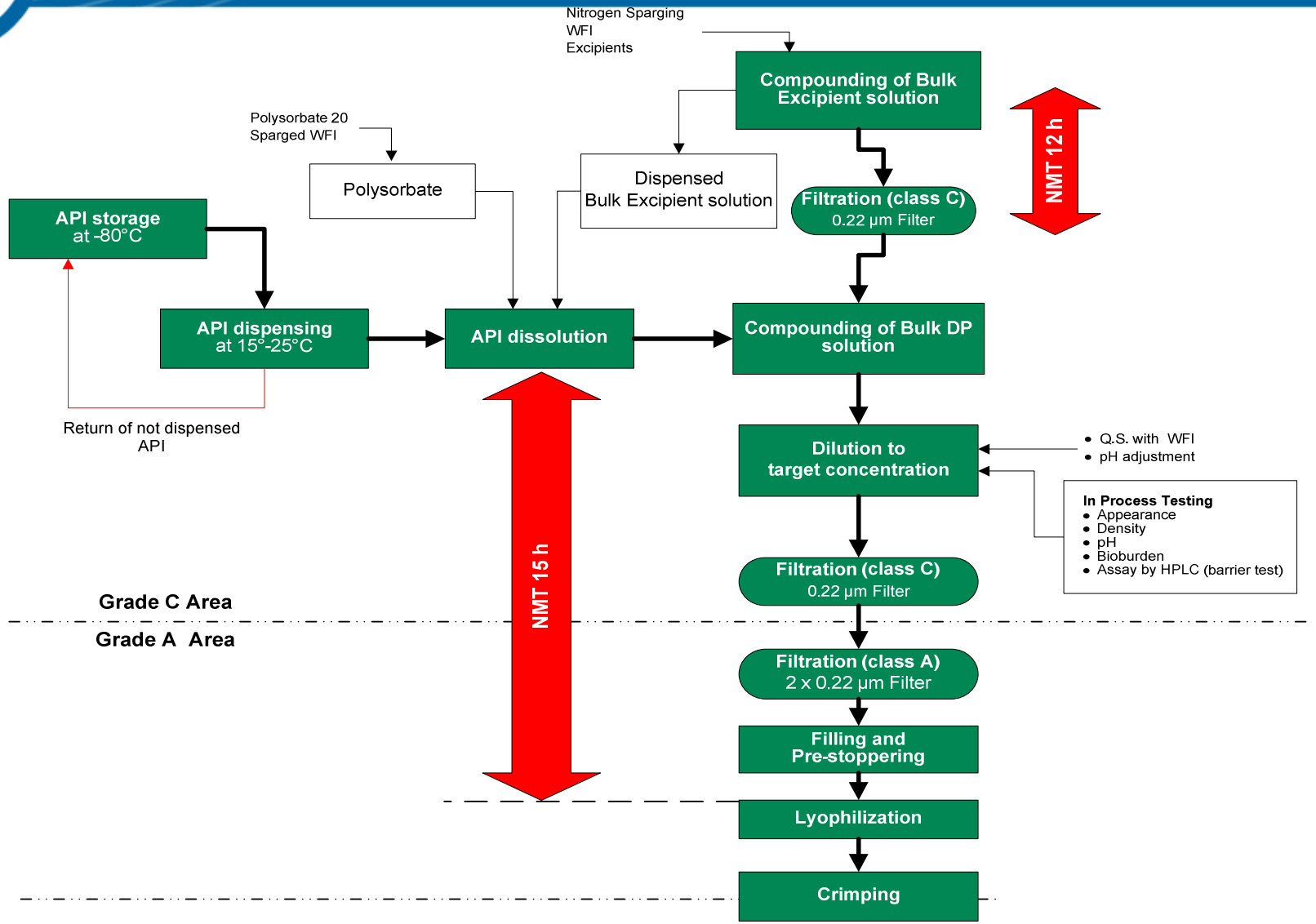
- ❑Group 1. Thinking as Prj manager, define your idea of Value for the Project team
- ❑Group 2. Thinking as Project team member, define your expectation from the Prj Manager

Workshop 5 process transfer case study

Technology Transfer

Product	YYY	
API and Pharmacological use	No special RA concern categories	
Pharmaceutical dosage form	Sterile lyophilized DP. 0.0050 mg/vial	
Product phase	Commercial	
Unit Dose composition	•API: 5.0 mg •Polysorbate 20: 0.8 mg •Sucrose:190.0 mg •Potassium Phospate, Dibasic: 18.0 mg	•Citric Acid: 22.8 mg •Phosphoric Acid: 7.0 mg •Vit E: 0.008 mg
Fill Volume (Including overfill)	10 mL	
Batch Size	120K Vials	
API Storage condition	-70°C	
Finish Product Storage	2-8°C	
Finish Product Shipment	2-8°C	

Technology Transfer



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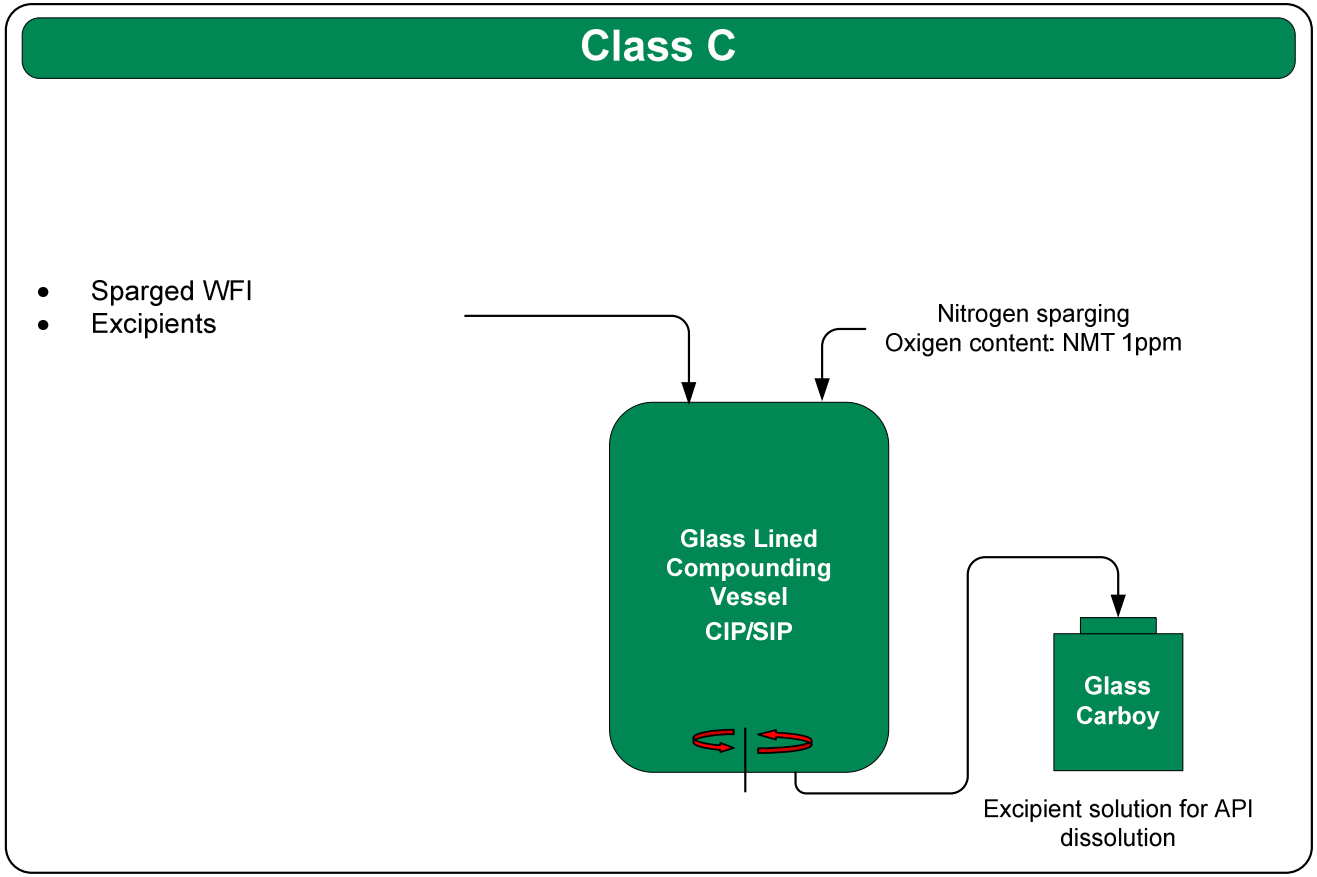

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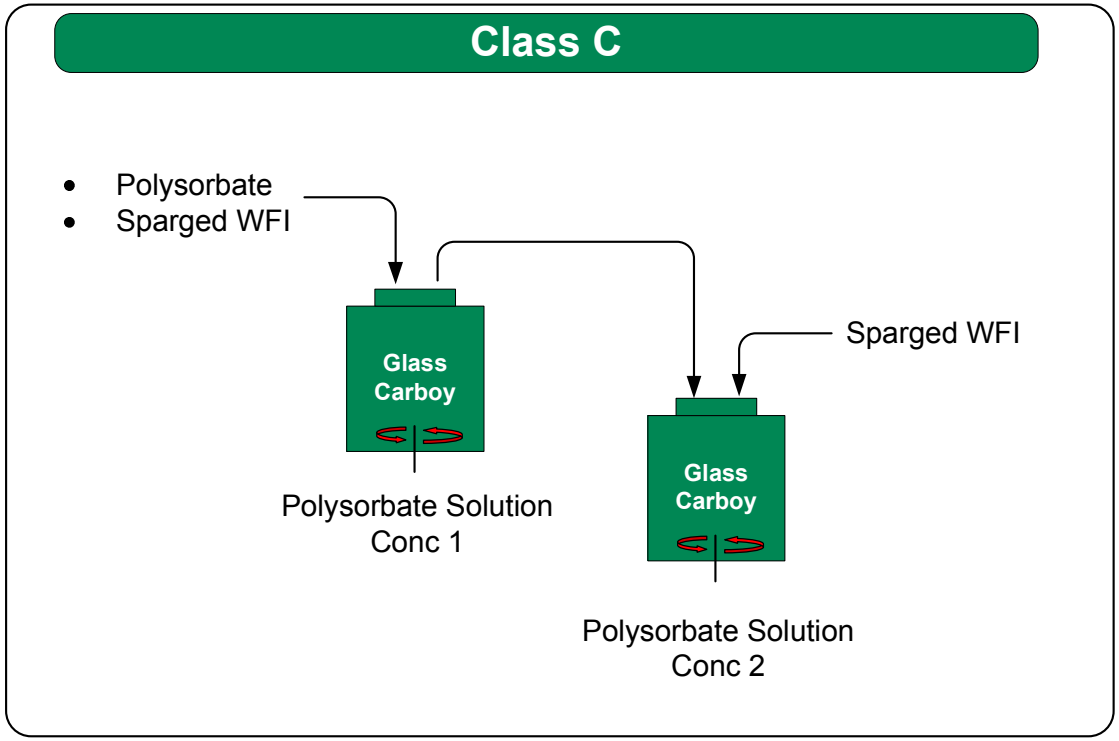

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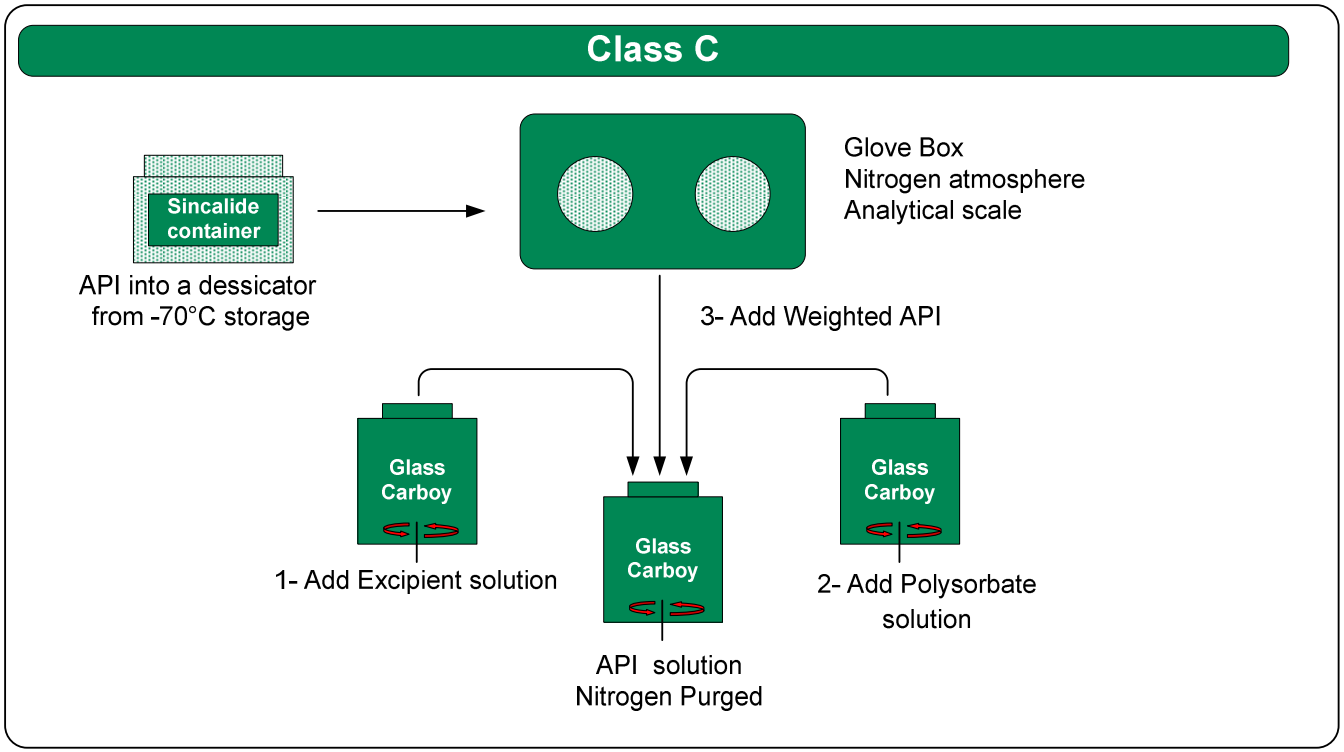

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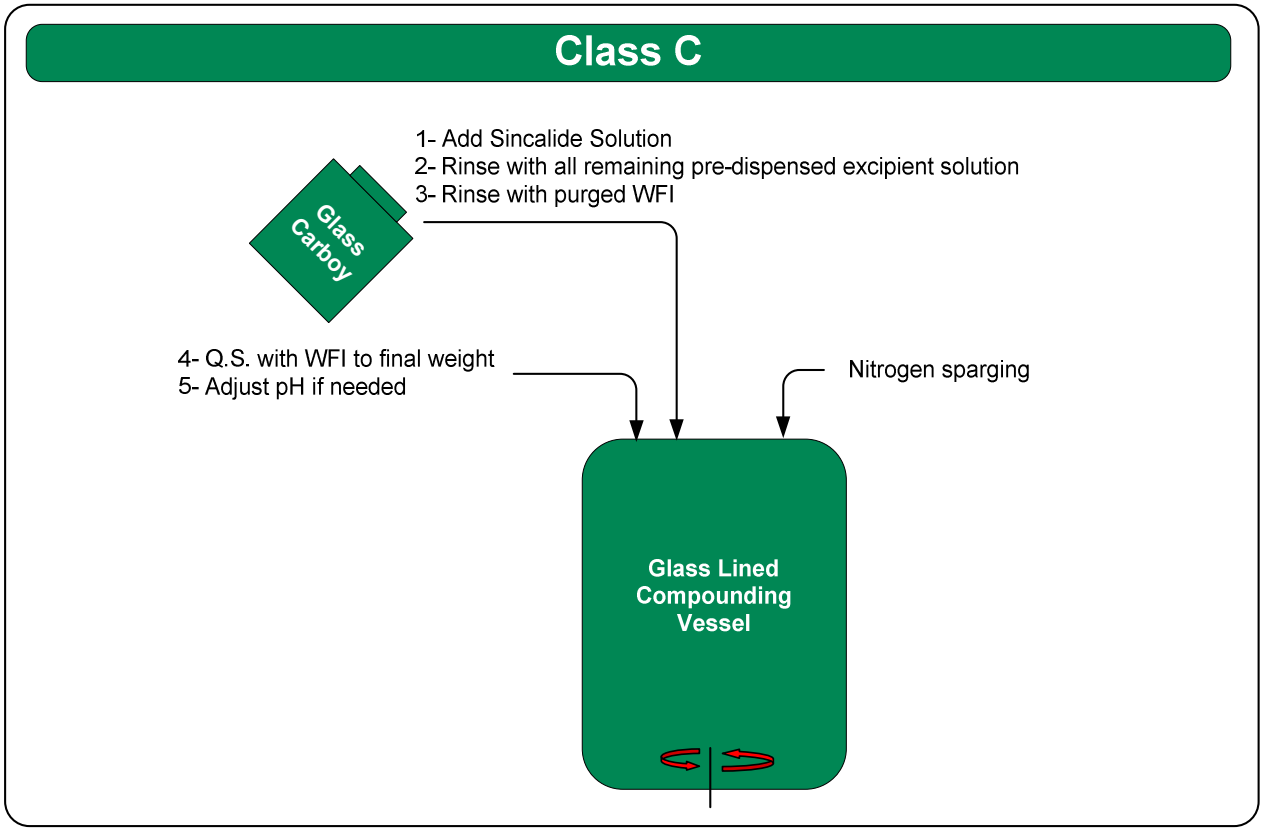

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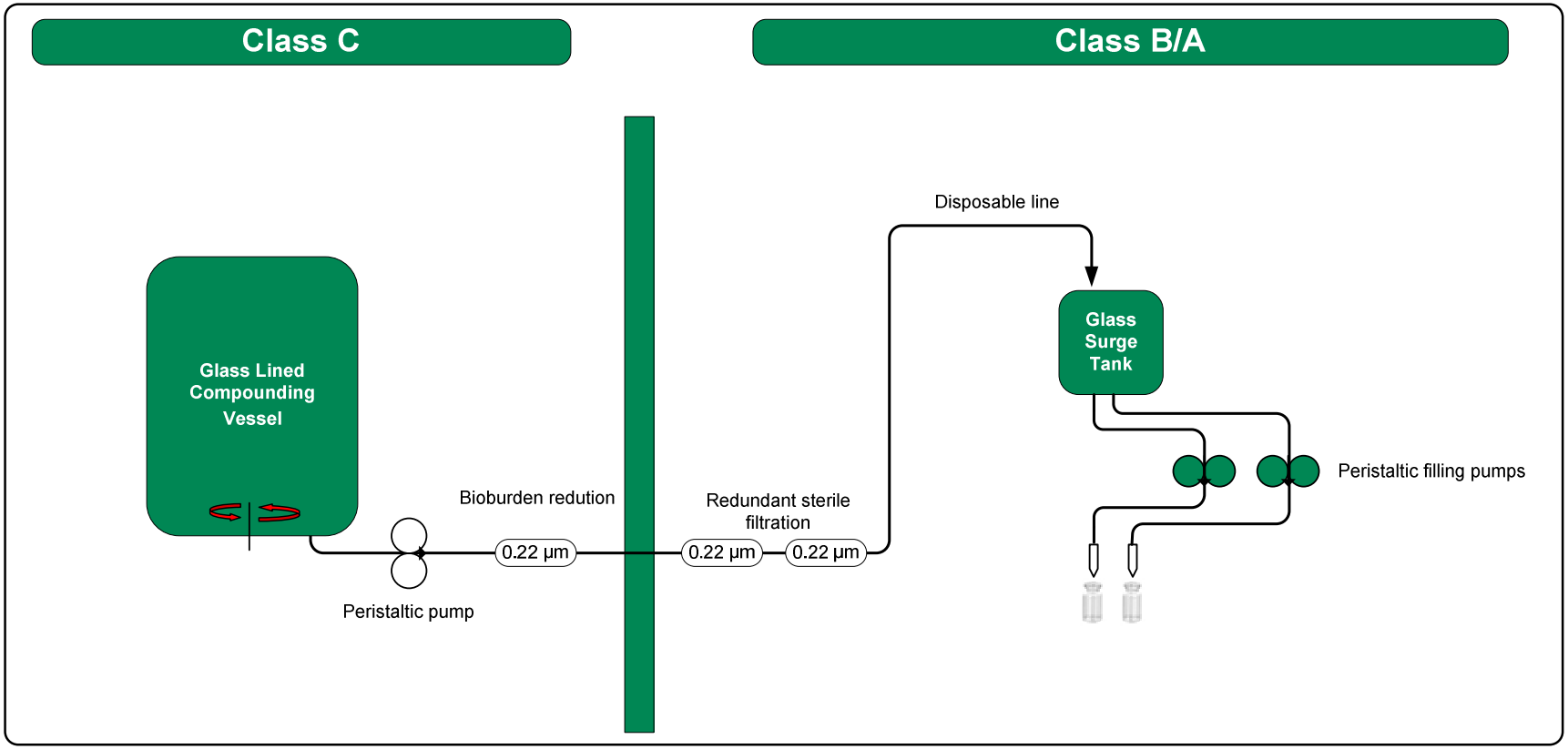

Technology Transfer

Product Quality Attributes
Micro Attributes Endotoxins Sterility
Chemical & Physical methods • Moisture content by KF • Appearance of the solution (after reconstitution) • Density of the solution (after reconstitution) • pH of the solution (after reconstitution) • Appearance and colour of lyophilized cake (DP) • Particles of the solution (after reconstitution) • Oxygen in headspace of drug product vial (CCI test). • Uniformity of dosage units • Cosmetic appearance of the cake • Impurity profile and assay • Amorphous at X ray of the cake

Technology Transfer

❑**Background:**

A product dedicated to EU market, has to be outsourced from one of your site in US. The manufacturing history of the product in the current manufacturing site is not robust.

The partner has been identified and selected. Agreement is in place…

❑**Questions**

- ❑Define the Process Variables
- ❑Prepare a Risk Assessment based on the quality attributes defined by the SU and the Process Variables identified by the RU

Benchmarking

- Technology transfer Organization in your company
- Technology Transfer Leader
  - Description of the role in the TT Projetc
  - Skills
  - Background
- TT project duration
- Interaction with the “site” – when and how