Sept 29th and 30th , Mirko Gabriele

Managing Technology Transfer Projects in Pharma

Today's Agenda

14:00 **Attendees Introduction and Course Expectations**

14:10 **Course Introduction**

14:15 **Pharma Management**

- What is a project in pharma? Main principles & final scope
- Regulatory & Quality Framework
- Pharma project lifecycle and main steps (Project Matrix)
- Terminology

15:00 **Team Role in Pharma**

- Org Chart approaches
- Functions RACI in each single step

15:30 **Project Management Role in Pharma Technology Transfer Projects**

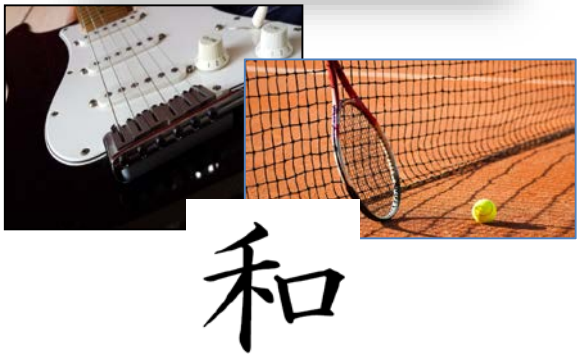
- Technology Transfer as key example of a pharma project
- Skills
- Leadership styles

16:00 **Pharma Tech Transfer Projects Governance**

- Governance standard approach in pharma
- Project Governance Tools
- Timelines definition
- Planning and execution control tools
- Performance indicators
- Project Closure

17:00 **Q&A & Day 1 Closure**

About myself…



How I'm used to introduce myself

- *Pharmaceutical Chemist with MBA in Pharma Administration. Qualified Person since July 2015*
- *QC and R&D as first steps in my career then my true love: Patheon TT & BM since 2008*
- *TT PM, BM, TT Manager, Global TT Sr Manager, DPS*
- *Production Director since May 2017*
- *Next steps…Who knows??!*

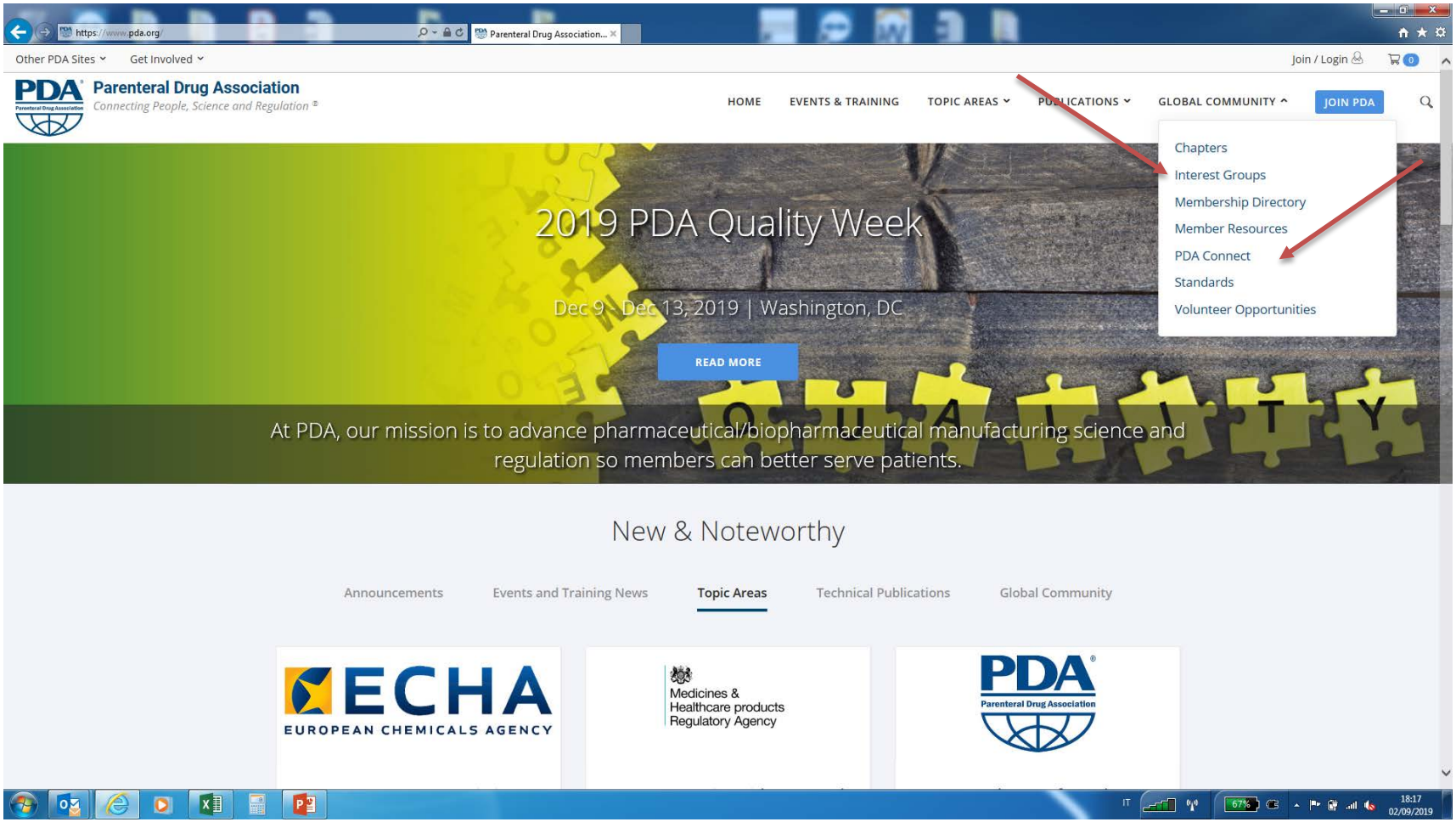
What the others say about me

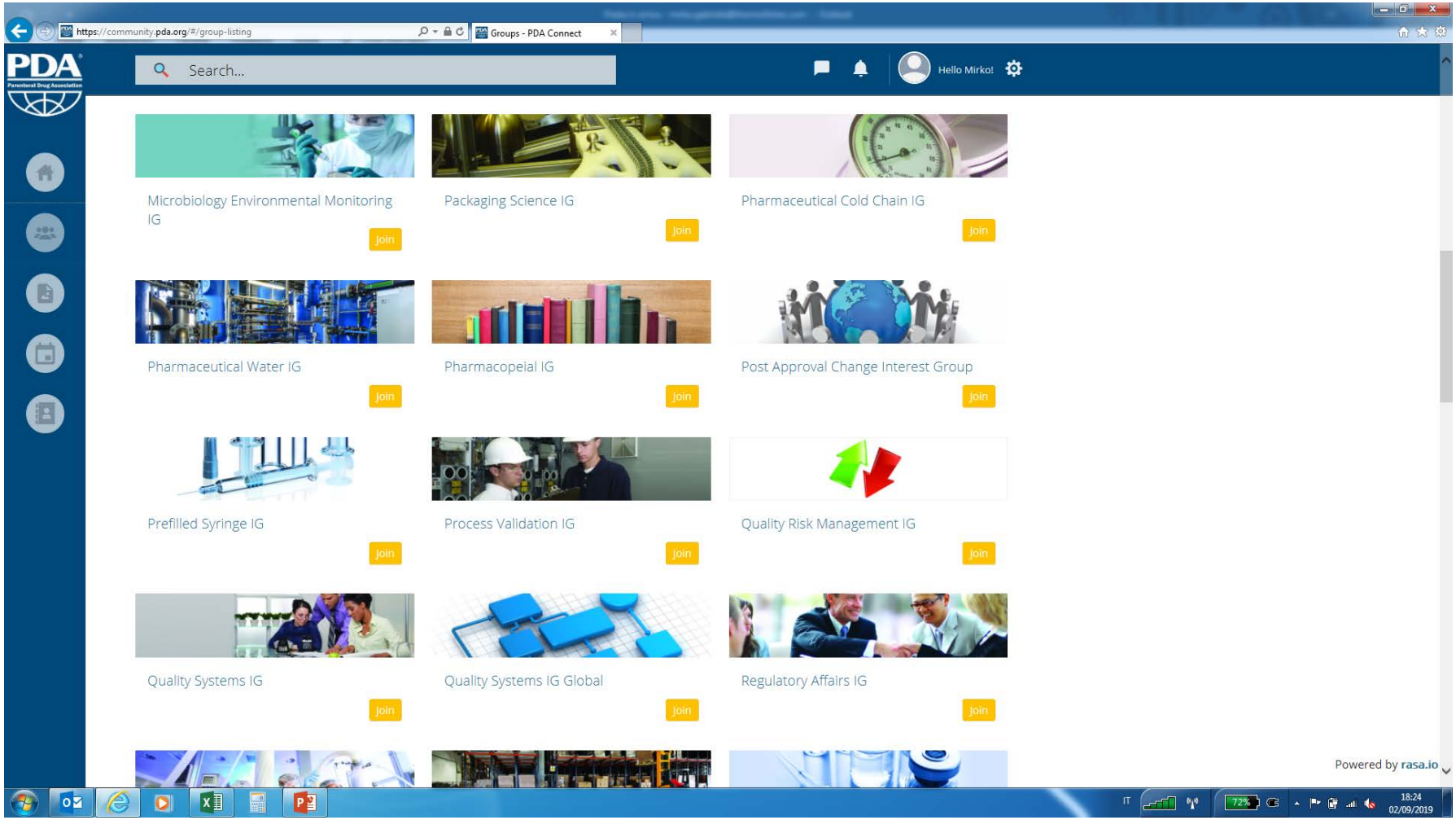
- *You will rock being yourself*
- *One of the Best dressed man in the network (after Jim and Franco and some others…)*
- *Highly motivated and passionate about work…always hungry about Knowledge!*
- *Guilt-ridden…no matter how much he is accomplishing…never enough*
- *Visionary…always! Demotivating him? No way!*
- *Stubborn but… (my wife voice)*
- *Great dad (my personal interpretation of Andrea's smile – my kid 2 years old!)*

About my PDA life

- *Team Leader for TR65 issuing*
- *PDA RAQAB Members since 2014*
- *PDA TT IG European Leader and European trainer on TT topics since 2016*
- *PDA Italy members*

Technology Transfer IG Session: About the IG

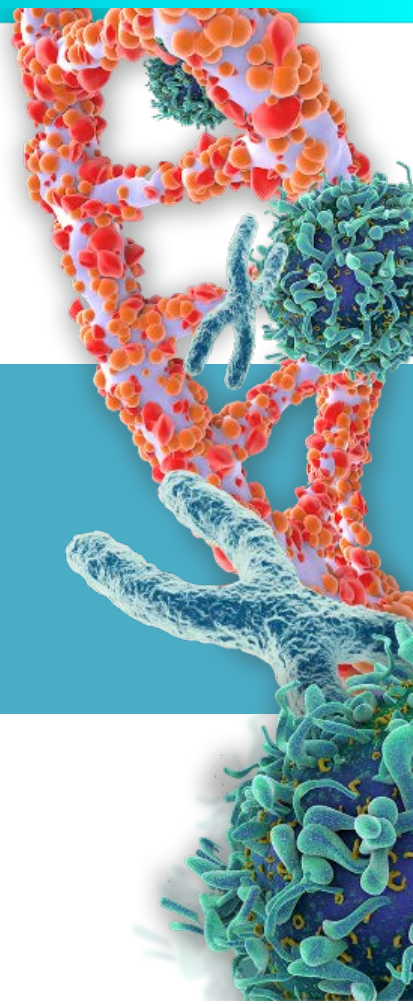



https://community.pda.org/#/group-listing
Groups - PDA Connect
Search...
Hello Mirko!
Microbiology Environmental Monitoring IG
Join
Packaging Science IG
Join
Pharmaceutical Cold Chain IG
Join
Pharmaceutical Water IG
Join
Pharmacopeial IG
Join
Post Approval Change Interest Group
Join
Prefilled Syringe IG
Join
Process Validation IG
Join
Quality Risk Management IG
Join
Quality Systems IG
Join
Quality Systems IG Global
Join
Regulatory Affairs IG
Join
Powered by rasa.io
18:24
02/09/2019

PDA Parenteral Drug Association

Who we are…

Mission: We enable our customers to make the world healthier, cleaner and safer.



$22B
in revenues

50
countries

>$900M
R&D investment

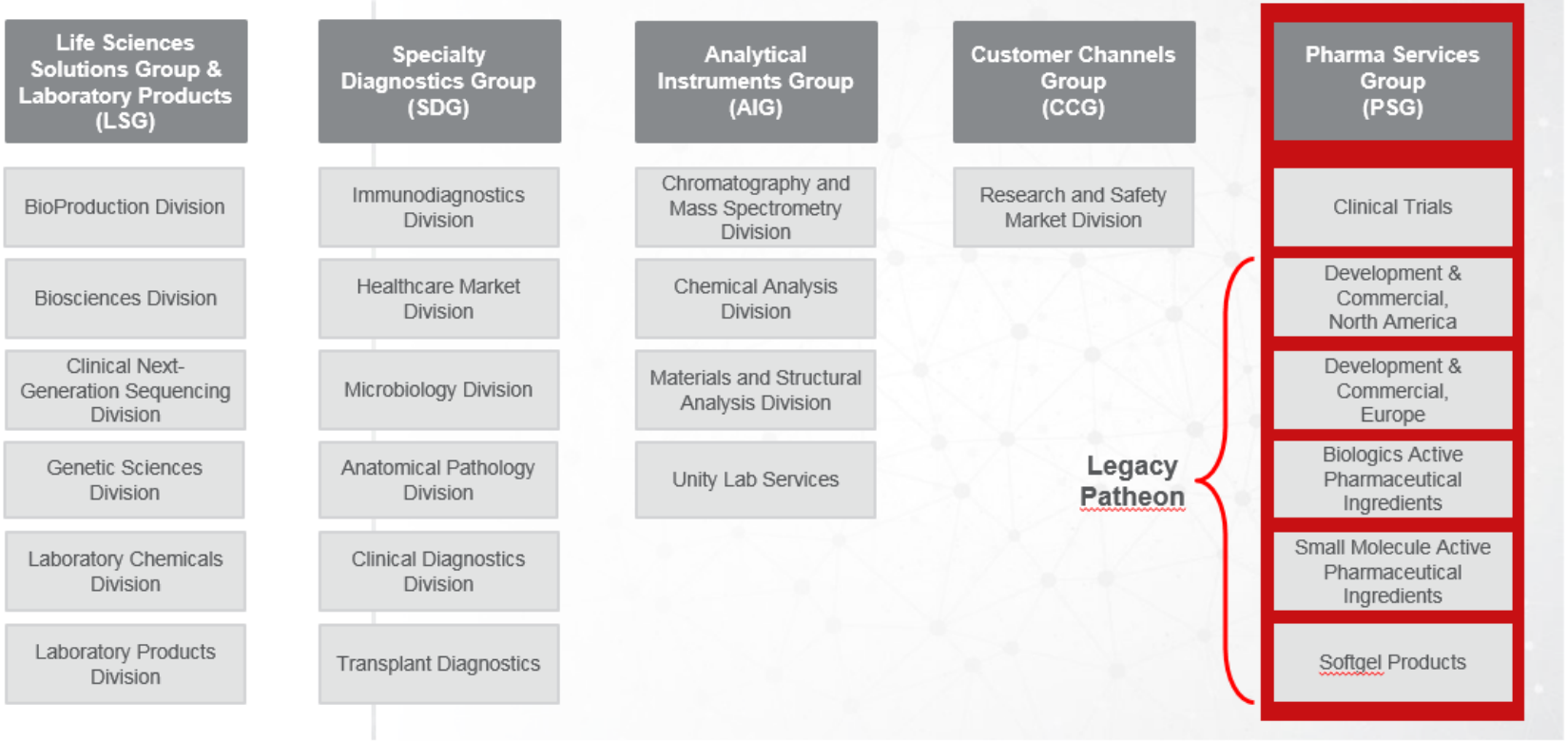
>70,000
employees

Our Customer Focus:
We help accelerate innovation and enhance productivity for our customers.

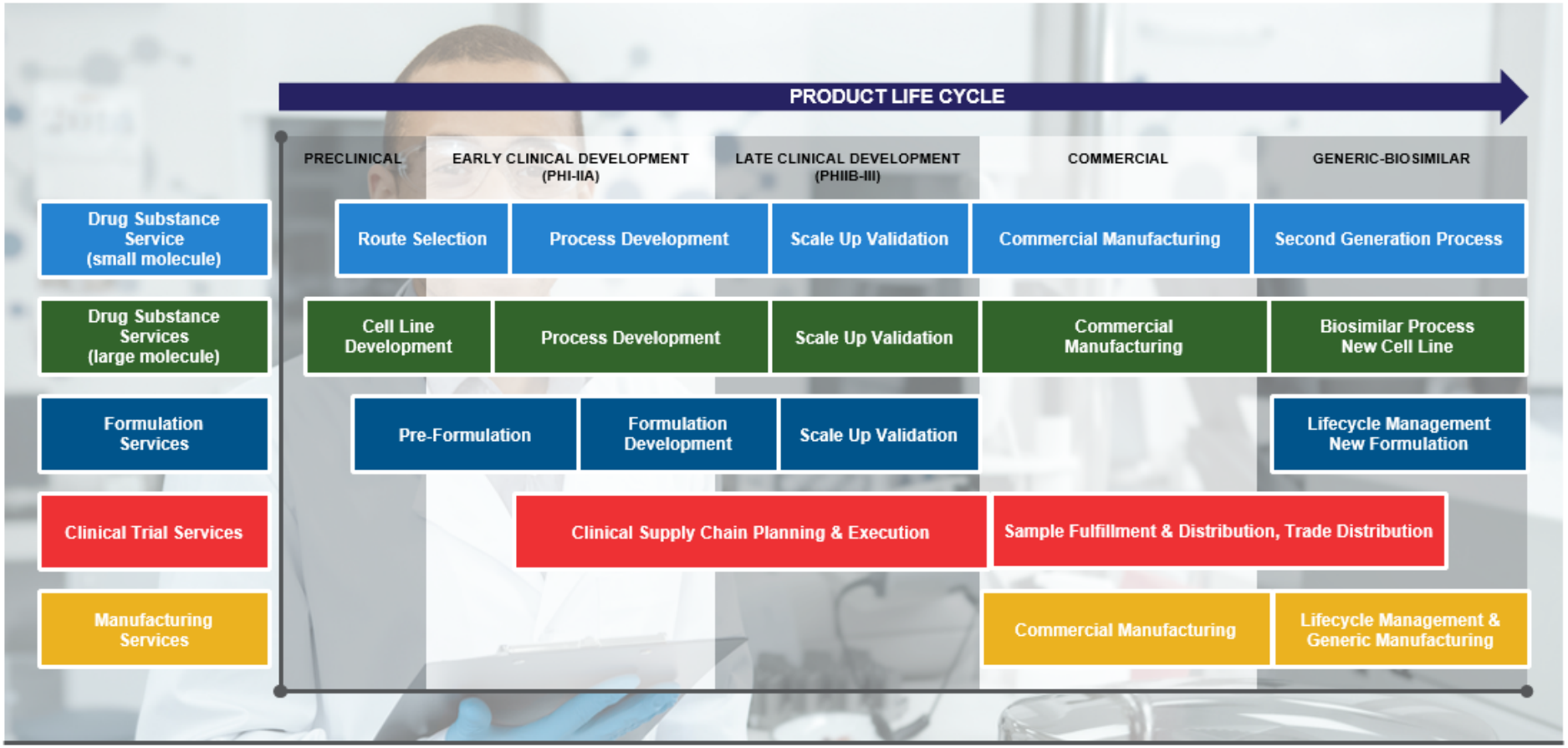
ThermoFisher SCIENTIFIC

thermo scientific | applied biosystems | invitrogen | fisher scientific | unity lab services

Who we are…


Life Sciences Solutions Group & Laboratory Products (LSG)
BioProduction Division
Biosciences Division
Clinical Next-Generation Sequencing Division
Genetic Sciences Division
Laboratory Chemicals Division
Laboratory Products Division
Specialty Diagnostics Group (SDG)
Immunodiagnostics Division
Healthcare Market Division
Microbiology Division
Anatomical Pathology Division
Clinical Diagnostics Division
Transplant Diagnostics
Analytical Instruments Group (AIG)
Chromatography and Mass Spectrometry Division
Chemical Analysis Division
Materials and Structural Analysis Division
Unity Lab Services
Customer Channels Group (CCG)
Research and Safety Market Division
Legacy Patheon
Pharma Services Group (PSG)
Clinical Trials
Development & Commercial, North America
Development & Commercial, Europe
Biologics Active Pharmaceutical Ingredients
Small Molecule Active Pharmaceutical Ingredients
Softgel Products

Our Business



Why Join this training

$1T

Global Rx sales by 2020

$160B

Global pharma and biotech R&D spend by 2020

60 to 10

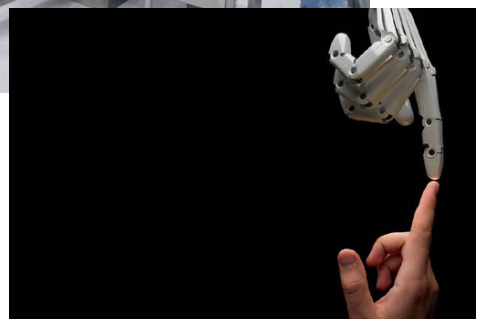
Shrink in number of Pharma players due to M&A in the last 20 years

TT IS AND WILL BECOME A MORE CRITICAL BUSINESS NEED, A "BEST TO BEST DEAL" WITH CUSTOMERS, TOP PLAYERS LOOKING FOR CDMO TOP PLAYERS

Why Discuss about TT

EVEN MORE TRUE, BASED ON PHARMA INDUSTRY DICHOTOMY PLANNED AS FUTURE SCENARIO

&



In other words…

- 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;
- **Business Opportunity** for big and small companies
- Project **complexity** is growing TT Experts have to be prepared to face challenges
- **Dynamic and challenge** environment

PMCO Program & TT IG

- TT was involved in the PDA PMCO program, as core activity of the Lifecycle Management of a Drug
- Get professionals experts in TT and define what RM means in TT;
- TR-65 was issue in August 2015
- TT Interest Group was started up in May 2016
- Training in Europe and US are organized yearly to maintain high the attention on this topic and to proceed defining best practices in TT
- TR-65 “revamping program”

My expectations for the two days…

- Meet new people
- Networking
- Share experience on TT
- Benchmarking on TT organization, Approaches
- Understand opportunity for improvements

What about you?

What is your expectation?

Pharma Management

What does project in pharma mean?

Technology Transfer 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)

Technology Transfer 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 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.

Good Transfer Practice → Good, Reproducible, Safe and Effective Manufacturing Practice → **Good & Safe Product delivered to the Patient**

Technology Transfer 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.

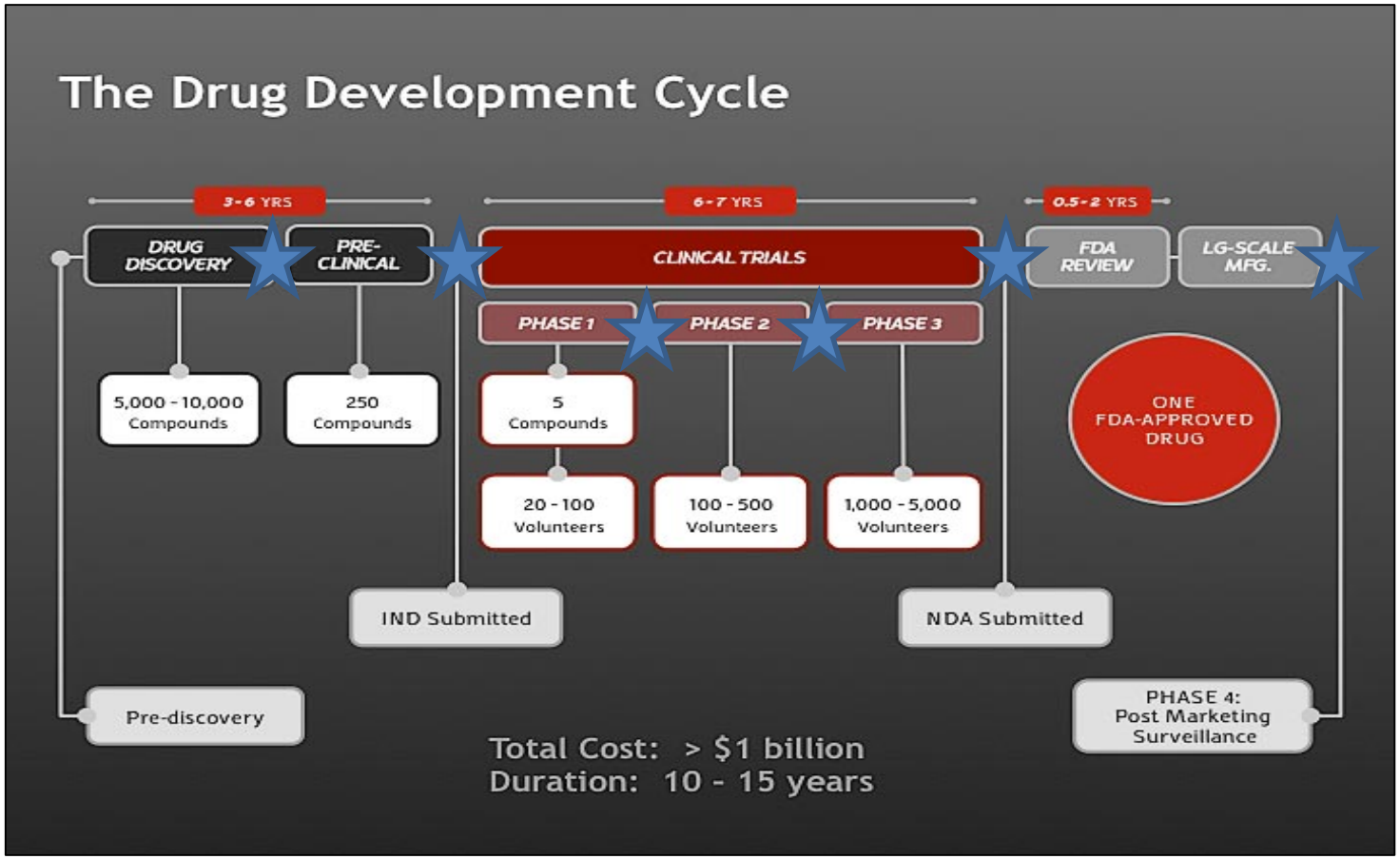
Technology Transfer main concepts

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).

Two main Risk Categories in Technology Transfer:

- *Project Risks*, associated with project management and people handling
- *Process Risks*, associated with technical issue during process execution

Technology Transfer – When?



Technology Transfer – When?

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*

Terminology

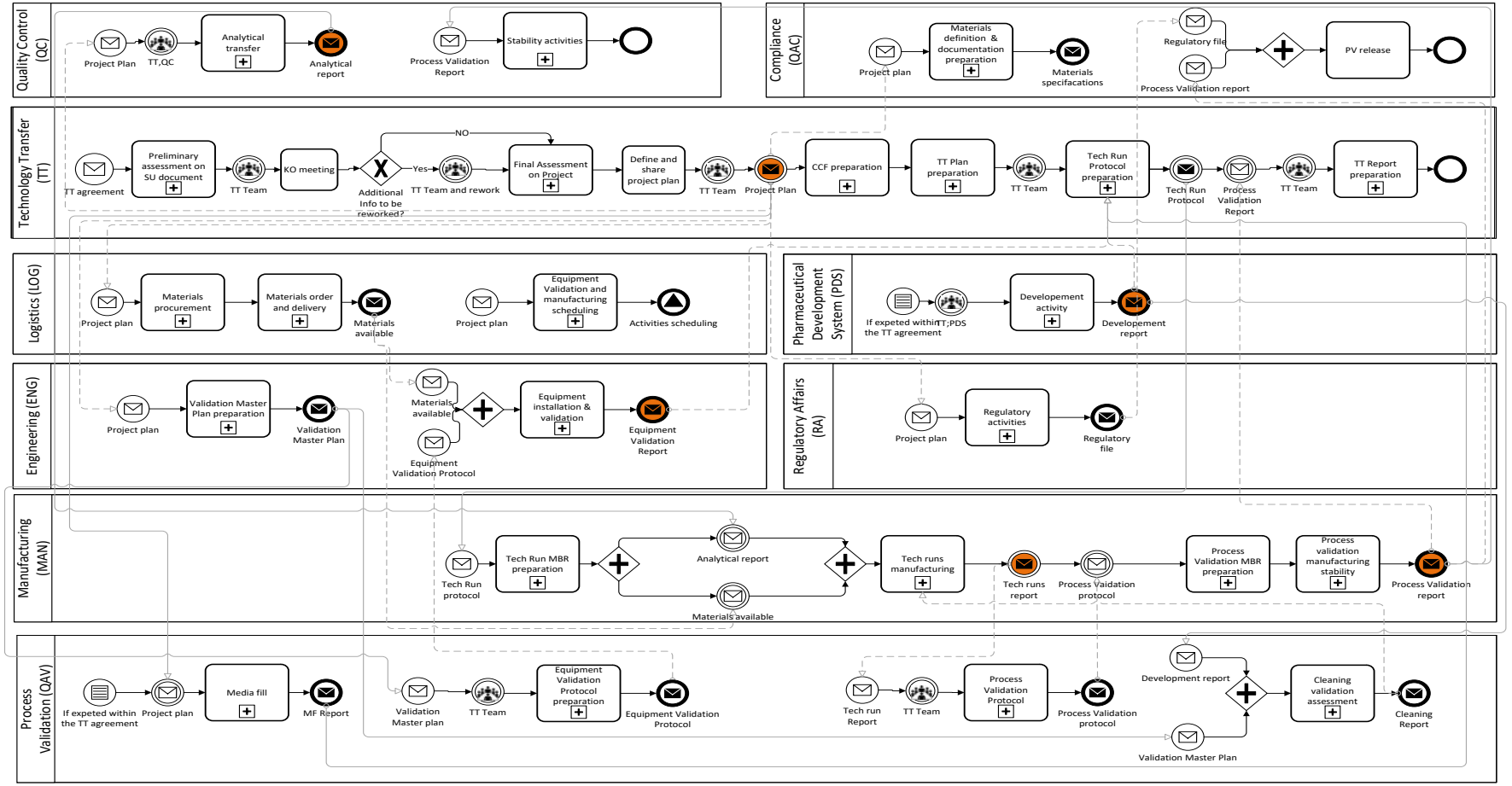
- **Primary Technology Transfer:**
  - From R&D to manufacturing site (industrialization process)
  - Intracompany/intercompany
- **Secondary Technology Transfer:**
  - From manufacturing site to manufacturing site
  - Intracompany/intercompany
  - Pre-submission, post-submission
  - Pre-commercialization, post-commercialization
- **Full or partial Transfer:**
  - Full manufacturing
  - Partial (analysis&release, secondary packaging etc)
- **Open transfer VS blind transfer**
- **Transfer IN vs Transfer OUT**

© Can Stock Photo - csp25964108

Terminology

- **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).
- **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.

Technology Transfer main concepts



Technology Transfer 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 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 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 main concepts

5 main steps!

4. Licensing & Manufacturing

a. Regulatory submission

b. Monitoring of the manufacturing batches

Technology Transfer main concepts

5 main steps!

5. Project Closure

a. Continuous improvement

b. Lesson learned

Technology Transfer main concepts

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 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 …in GMP

Technology Transfer 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

…under GMP!

Technology Transfer …in GMP

1. **EU GMP Guidance** for Medicinal Products for Human and Veterinary

   - Vol 4, chapter 1, 4, 6 (Close to TT approach and definition)

   - Vol 4, chapter III (Quality aspects, ie QAA, Management review)

2. **FDA Guidance** for Industry in Contract Manufacturing Arrangements for Drugs

3. **WHO Guidance** on TT in pharmaceutical manufacturing n.961, 2011

4. **TR-65 PDA**

5. **ISPE Technical documentation**

…under GMP!

34

Technology Transfer …in GMP

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.

Appropriate level of training in place

…under GMP!

Technology Transfer …in GMP

- 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 …in GMP

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 …in GMP

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 …in GMP

SOP for TT Protocol/report handling

- ❑ 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
- ❑ Chapter 4. *Project identification:* procedure (codes, numbering)
- ❑ Chapter 5. *Project planning tools*
- ❑ Chapter 6. *Project monitoring tools*
- ❑ *Chapter 7. Project closure tools*
- ❑ *Chapter 8. Document History*
- ❑ *Appendix. Template and signature page*

- ❑ Chapter 4. Project Story
- ❑ *Chapter 5.* Project Results
- ❑ *Chapter 6.* Lesson Learnt and CPV
- ❑ Chapter 7. Document Closure
- ❑ Chapter 8 . Document History

Take Away

What does project in pharma mean?

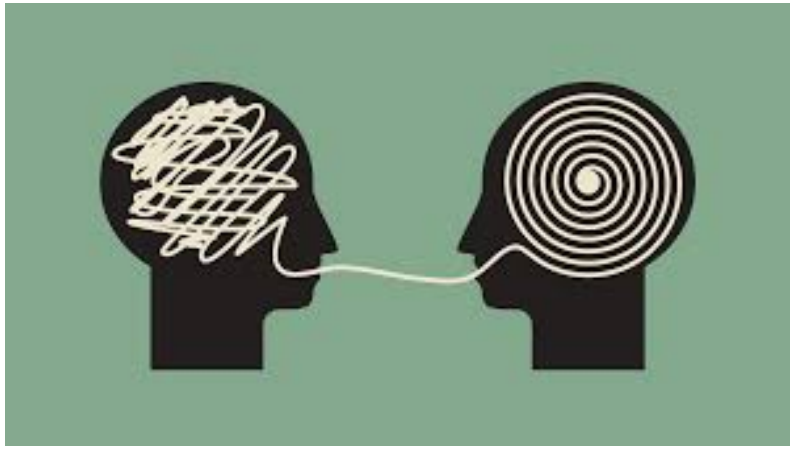
- *Multidisciplinary Context*
- *Be always focus on Patient as this is our final «Client»*
- *Dynamic and challenging environemnt*
- *5 main risks categories to be considered*
- *Map your internal & external factors to be sure we are taking the TT under control*

Team role in pharma

Is the team critical for TT Project success?

Team role in pharma

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).

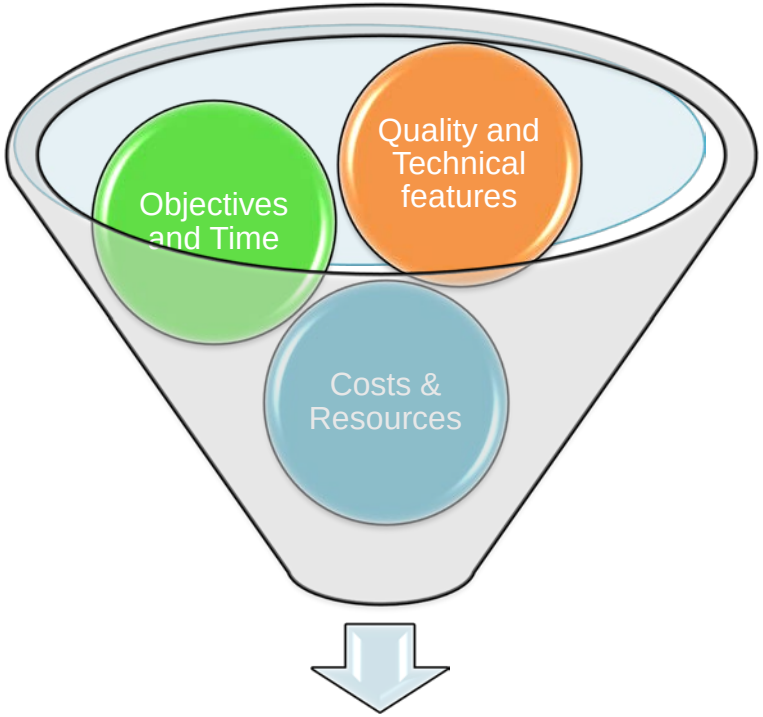


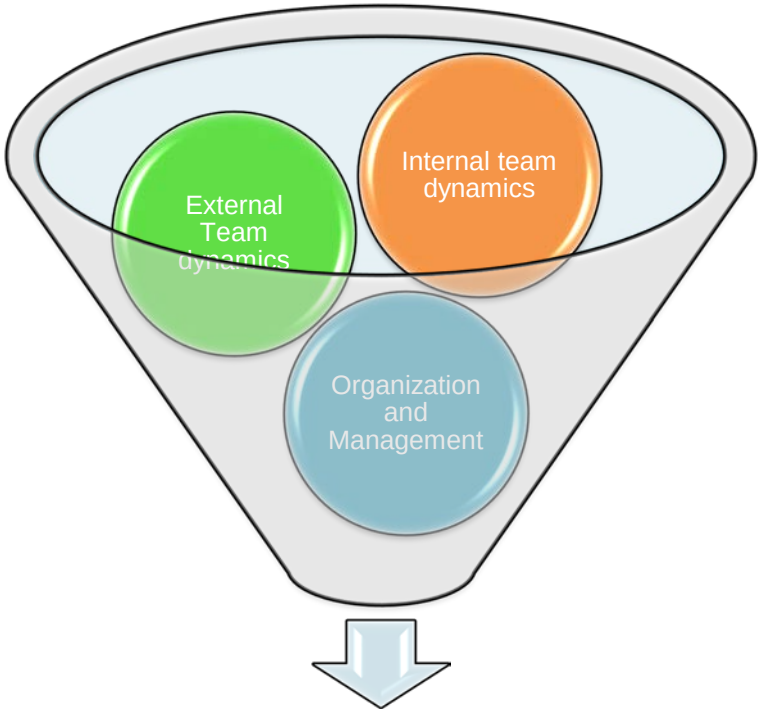
Team role in pharma

Which are the main Project risks? – PDA TT IG 2018

1. *Project Scope missed or misunderstood*
2. *Underestimating of new site/process impact on product attribute*
3. *Lack of product/ process understanding*
4. *Lack of communication*
5. *Lack of escalation process*
6. *Wrong extimation of time/resources/costs*
7. *Lack of engagement of Team members*
8. *Lack of performance monitoring during execution*

Team role in pharma

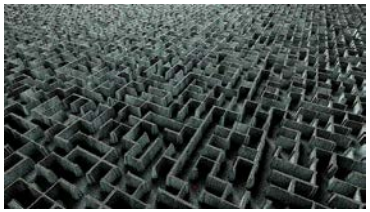




Planning

Social Intelligence

Team role in pharma



Business

Regulatory Affairs

Manufacturing

Project Engineering

- *At each project phase, different functional areas need to interact to provide specific deliverables.*
- *Cross-functionality is a key component of all technology transfers requiring involvement from a wide range of functional areas*

Quality

Development

Process Engineering

Regulatory

Supply Chain

Procurement

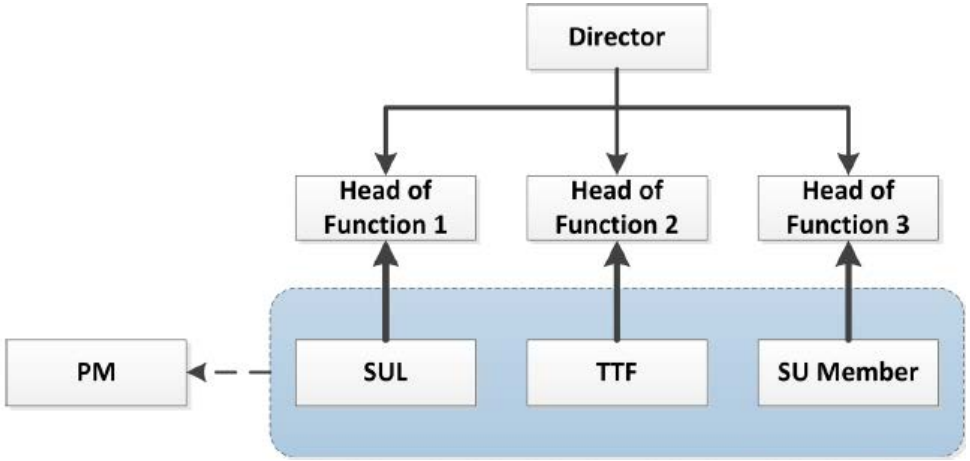
Analytical

Team role in pharma

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.

Two main organizational model are seen in the pharma environemnt: *light matrix* and *hard functional*

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

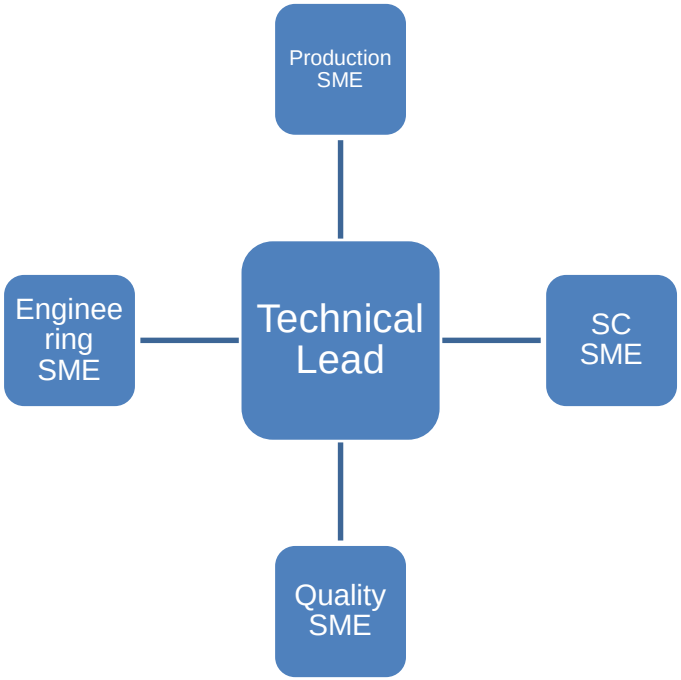


46

Team role in pharma

In a hard functional approach, a «Business Unit» is created around the technology transfer needs. Main SMEs report directly to the Technical Lead with a «silos» approach.

Typical of small companies with few TTs per year, it seems to be the best way to provide hard control of well defined and specific activities in a routine and standardized environment.



47

Team role in pharma

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.

Team role in pharma

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

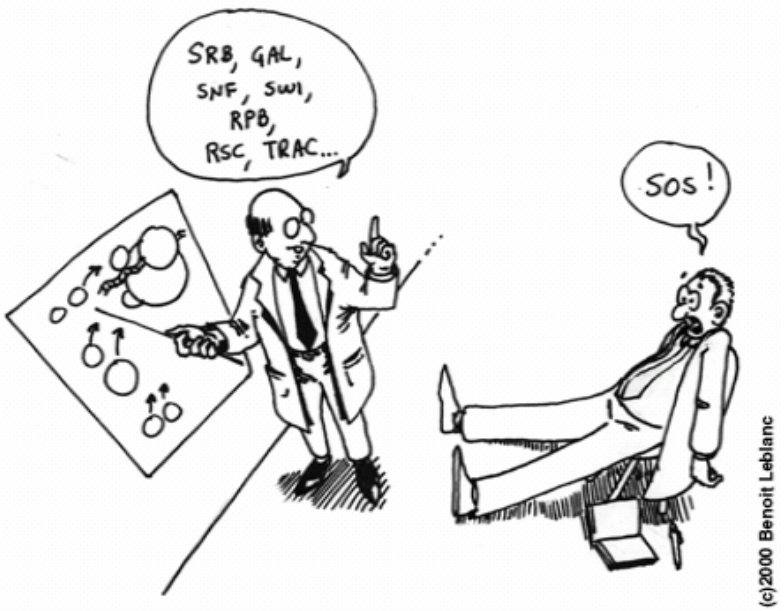
Team role in pharma

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!

Team role in pharma

#	Meeting	Attendees	Frequency	Tentative Duration (min)	Purpose	Tool	Deliverables
1	Intra Company alignment	SU Leader RU Leader	Weekly/Biweekly based on project step	30	Alignment between Receiving Units and Sending Units in terms of evaluation/plans/actions	Project Dashboard	Meeting Minutes
2	Project Meeting	RU Leaders SU PM (or equivalent role)	Weekly	30	Discussion between PMs on Project status and execution, performance and communication between teams, main risks to be mitigated to avoid delay or stops	Project Dashboard Project Plan Risk Register	Meeting Minutes
3	Technical Meeting	RU Leader SU PM (or equivalent role) SMEs from parties based on agenda	Weekly	60	Detailed technical discussion on project tasks or issues	Technical Documents Project Plan Risk Register Project Dashboard	Meeting Minutes Risk Register updated Project Dashboard updated
4	Internal Sponsor meetings	SU Leader RU Leader RUSponsor	Biweekly	30	Update the project sponsor on Project status , SU relationship, RUteam performance and needs, risks and mitigation plan, issues and related action on going for resolution	Project Dashboard Risk Register	N/A
5	Project Sponsors Meetings	RUSponsor SU Sponsor RU Leader SU PM (or equivalent role)	Monthly	30	Update the SU/RUSponsors on the Project status, Relationship, Team performances, risks and needs	Project Dashboard Risk Register	Minutes

Team role in pharma

Stakeholders are individuals and groups, both inside and outside the Challenge team/start-up, who can:

-influence the success of the business plan and start-up

-be impacted by the new start-up

-actively support the start-up through funding, mentoring, etc.

- they are internal or external to the team/start-up

Team role in pharma

Suppliers

SU Team Members

Unions

Upper Management

Regulatory Agency

RU Team Members

Competitors

Corporate Experts

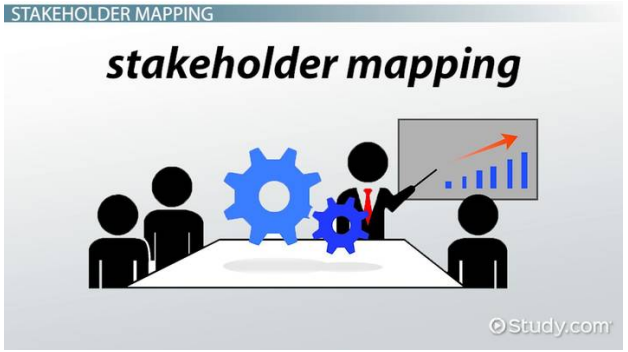
Employees

Business Partners

Team role in pharma

Stakeholders are individuals and groups, both inside and outside the Challenge team/start-up, who can:

- influence the success of the business plan and start-up
- be impacted by the new start-up
- actively support the start-up through funding, mentoring, etc.
- handling of group dynamics is fundamental for process success
- they are internal or external to the team/start-up
- Stakeholder mapping is a key pharma process step
- Several tools are available to facilitate stakeholder mapping



Team role in pharma

The Stakeholder Analysis Process – tool 1

1.**Brainstorm** a list of Stakeholders, asking, “who can influence the success of my business plan and startup and who can be impacted by the project?” Segment the stakeholders into meaningful clusters as appropriate (functions, regions,etc.)

2.Ask, “to what degree do they have the ***power to influence the success*** of the ultimate startup?” Use the 1-5 scale shown on the Template (COLUMN 0)

3.Next ask, “what is this stakeholder’s current ***level of commitment to the startup***? How Favorably do they view the startup?” Use the 1-5 scale shown on the Template (COLUMN P)

4.Ask, “for our start-up, what does success look like to this stakeholder, what would ***they consider to be wins***?” (COLUMN T)

5.Identify **proactive actions** to achieve these “wins”, and to engage them to increase their favorability.

Team role in pharma

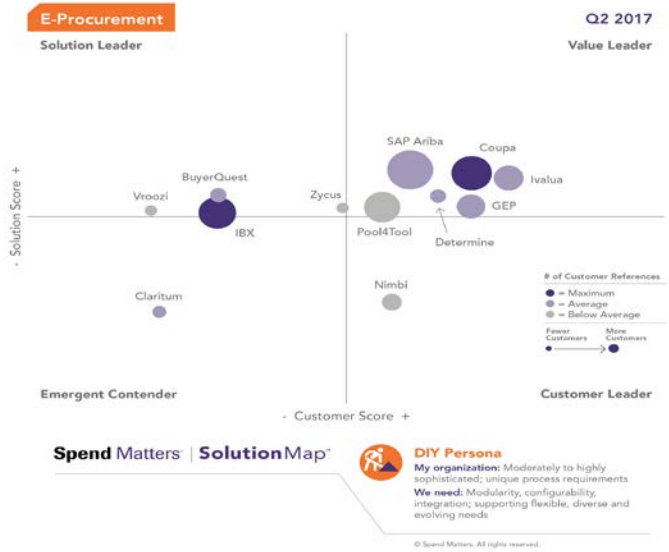
The Stakeholder Analysis Process – tool 2

1.**Brainstorm** on Stakedolders Dynamics

2.Track them with colored lines (influences, Defers, Antagonizes)

3.Track Power Level of each stakeholder identified

5.Identify **proactive actions** to achieve these “wins”, and to engage them to increase their favorability.

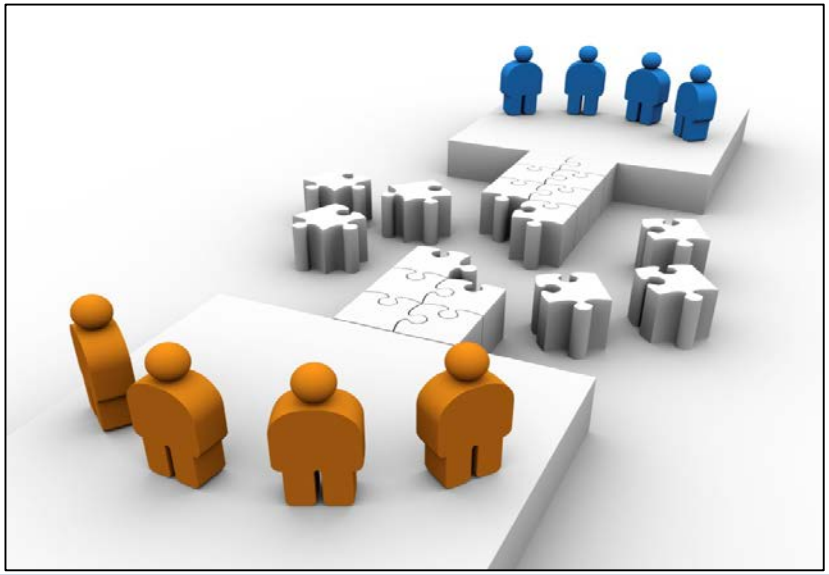


PM Role in pharma tech transfer projects

Is the PM critical for TT Project success?

PM Role in pharma tech tranfer projects

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



PM Role in pharma tech tranfer projects

– **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

PM Role in pharma tech tranfer projects

Role / Project Deliverable (or Activity)	Project Leadership									
	Technology Transfer (TT)	Business Managment (BM)	Quality Control (QC)	Quality Compliance (QAC)	Logistics (LOG)	Engineering & Equipment Validation (ENG)	Manufacturing (MAN)	Process & Cleaning Validation (QAV)	Regulatory Affairs (RA)	Pharmaceutical Development System (PDS)
Preliminary assessment	A/R	A/R	C	C	I	C	C	C	C	I/C
Meet the customer and verify information	A/R	A/R	I	I	I	C/I	I	I	C	I/C
Define and share the project plan	A/R	I/C	I	I	I	C/I	I	I	I	I
Change Control Form preparation	A/R	I/C	C	R/C	C	I	C	C	C	C
Technology Transfer Plan preparation	A/R	I/C	C	C	I	I	C/I	C/I	C	I
Tech run protocol preparation	A/R	I/C	C	I/C	I	I	C/I	C/R	I	I
Technology Transfer Report preparation	A/R	I/C	I	I	I	I	I	I	I	I
Analytical transfer	I/C	I	A/R	I/C	I	I	I	I	I	I
Stability Activities	I/C	I	A/R	I/C	I	I	I	I	I/C	I
Materials definition & documentation preparation	I/C	I/C	I	A/R	I	I/C	I/C	I/C	I	I
PV release	I/C	I/C	I	A/R	R	I/C	R	I/C	I/C	I
Materials Procurement	I/C	I/C	I	I	A	I/C	I	I		I
Materials Order and delivery	I/C	I/C	I	I	A	I/C	I	I		I
Equipment validation and manufacturing sheduling	I/C	I/C	I	I	R	A/R	I	I		I
Validation Master Plan	I/C	I	I	I	I	A	I/C	I	I	I
Equipment Installation and Validation	I/C	I	I	I	I/C	A	I/C	I	I/C	I
Tech run MBR preparation	I/C	I/C	I/C	I/C	I	I	A	I/C	I	I
Tech run manufacturing	I/C	I/C	I/C	I	R/C	I	A	I/C	I	I
Process Validation MBR preparation	I/C	I/C	I/C	I/C	I	I	A	C	I	I
Process Validation manufacturing stability	I/C	I/C	I/C	I	R/C	I	A	I	I	I
Regulatory activities	I/C	I	I	I	I	I	I	I	A	I
Development activities	I/C	I/C	I	I	I	I	I	I	I/C	A/R
Media Fill	I/C	I/C	C/R	I	R	I	R	A	I	I
Equipment Validation Protocol Preparation	I/C	I/C	I	I	I	A	I	I/C	I	I
Process Validation Protocol	I/C	I/C	C	I	I	I/C	C	A	I	I
Cleaning Validation assessment	I/C	I/C	C/R	I	I	I	C	A	I	I

60

PM Role in pharma tech tranfer projects

1. Transactional Leader

The best way to understand transactional leadership is to think of a typical transaction: **I give you this, and you do this in return.**

Pro: Confusion and guesswork are eliminated, because tasks and expectations are clearly mapped out by the leader.

Con: Due to the rigid environment and expectations, ***creativity and innovation are stifled***.

2. Transformational Leadership

Again, with this leadership style, it's all in the name: Transformational leaders seek to change (ahem, transform) the businesses or groups in which they lead by inspiring their employees to innovate.

These leaders are all about making improvements and finding better ways to get things done.

Pro: Leaders are able to establish a high level of trust with employees and rally them around a shared vision or end goal.

Con: In environments where existing processes are valued, this desire to change things up can ruffle some feathers.

PM Role in pharma tech tranfer projects

3. Servant Leadership

Servant leaders operate with this standard motto: ***Serve first and lead second***. Rather than thinking about how they can inspire people to follow their lead, they channel the majority of their energy into finding ways that they can help others.

Pro: This approach *boosts morale* and leads to a high level of trust, which results in better employee performance and a more positive company culture overall.

Con: *It's challenging*. Constantly pushing your own needs and priorities to the backburner isn't something that comes as second nature for most of us.

4. Democratic Leadership

You might also hear this leadership style referred to as "participative leadership." Leaders in this category run groups and projects like…well, a democracy.

Pro: *Creativity and innovation are encouraged*, which also improves job satisfaction among employees and team members.

Con: Constantly trying to *achieve consensus* among a group can be inefficient and, in some cases, costly.

PM Role in pharma tech tranfer projects

5. Autocratic Leadership

Autocratic leadership exists on the opposite side of the spectrum from democratic leadership.

You can think of this as a "*my way or the highway" approach*.

Pro: *Decisions are often made quickly and strategically*, and teams are kept on track as a result.

Con: *Employees can feel ignored, restricted*, and—in the absolute worst of cases—even abused.

6. Bureaucratic Leadership

Bureaucratic leadership goes "by the book," so to speak. With this leadership style, there's a *prescribed set of boxes to check in order to be a true leader*.

For example, bureaucratic leaders have hierarchical authority—*meaning their power comes from a formal position or title*, rather than unique traits or characteristics that they possess.

Pro: There's *plenty of stability*. Since this is a systematized approach to leadership, things remain constant even through personnel changes and other shifts that threaten to rock the boat.

Con: It's tempting to fall into the "we've always done it this way" trap. This *approach can be inflexible* and neglect to leave room for creativity or ideas from employees.

PM Role in pharma tech tranfer projects

7. Laissez-Faire Leadership

Do you remember the term "laissez-faire" from your high school French or history class? If not, let's refresh your memory. This is a French term that translates to "*leave it be*," which pretty accurately summarizes this hands-off leadership approach. It's the exact opposite of micromanagement.

Pro: This level of trust and *independence is empowering* for teams that are creative and self-motivated.

Con: *Chaos and confusion* can quickly ensue—especially if a team isn't organized or self-directed.

8. Charismatic Leadership

You know what it means to have a *lot of charisma*, and that's exactly what these leaders possess.

Charismatic leaders have magnetic personalities, as well as a lot of *conviction to achieve their objectives*.

Rather than encouraging behaviors through strict instructions, these leaders use eloquent communication and persuasion to unite a team around a cause.

Pro: Charismatic leaders are very inspirational and effective at getting an entire group invested in a shared objective.

Con: Due to their intense focus, it's easy for these leaders to develop "tunnel vision" and lose sight of other important issues or tasks that crop up.

PM Role in pharma tech tranfer projects

- **Is there a right style to lead a TT Project in pharma?**

NO because….

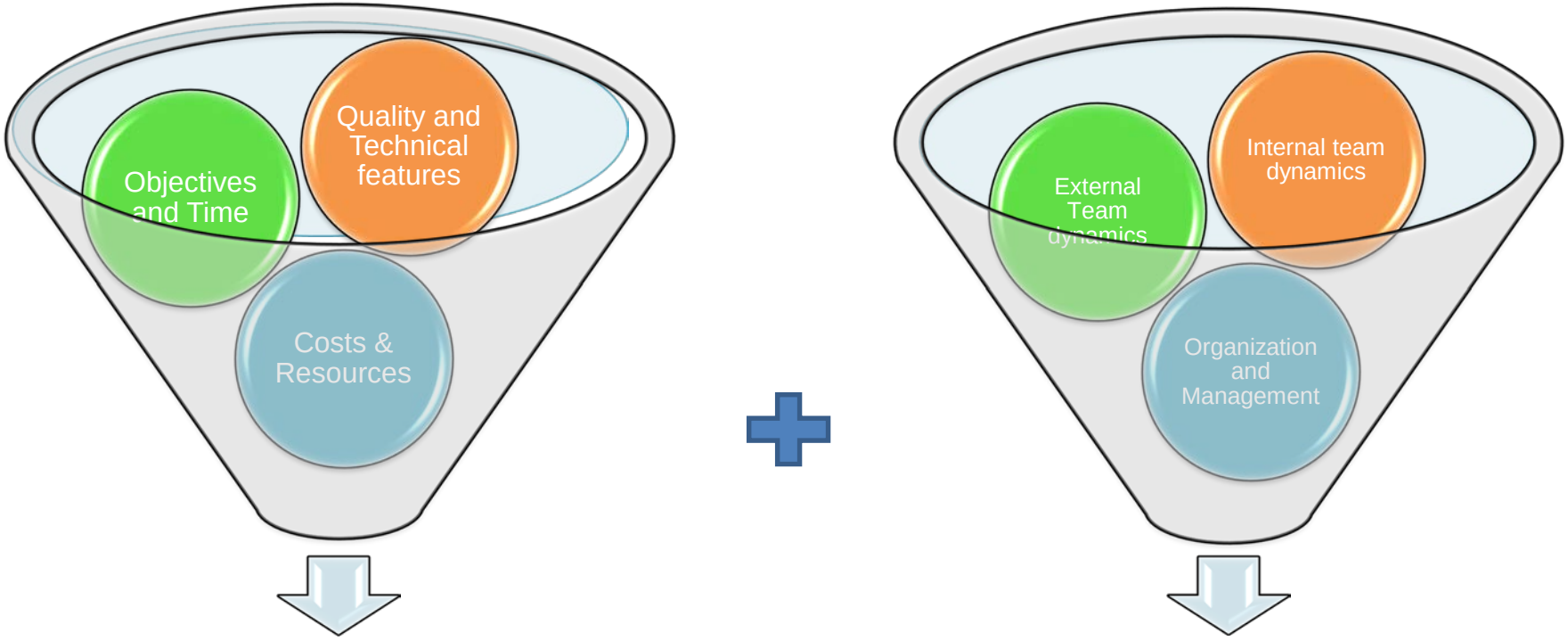
- Which is the best style I can use with this team?
- Which is the best style I can use in this situation?
- Which is the best style I can use with this RU or SU?
- What does it happen if I go against my Leadership Nature?

Get the best from your personal style and leverage human being resilience to be flexible where project requires it!

Pharma Tech Transfer Projects governance

Which does governance mean in TT?

Pharma Tech Transfer Projects governance

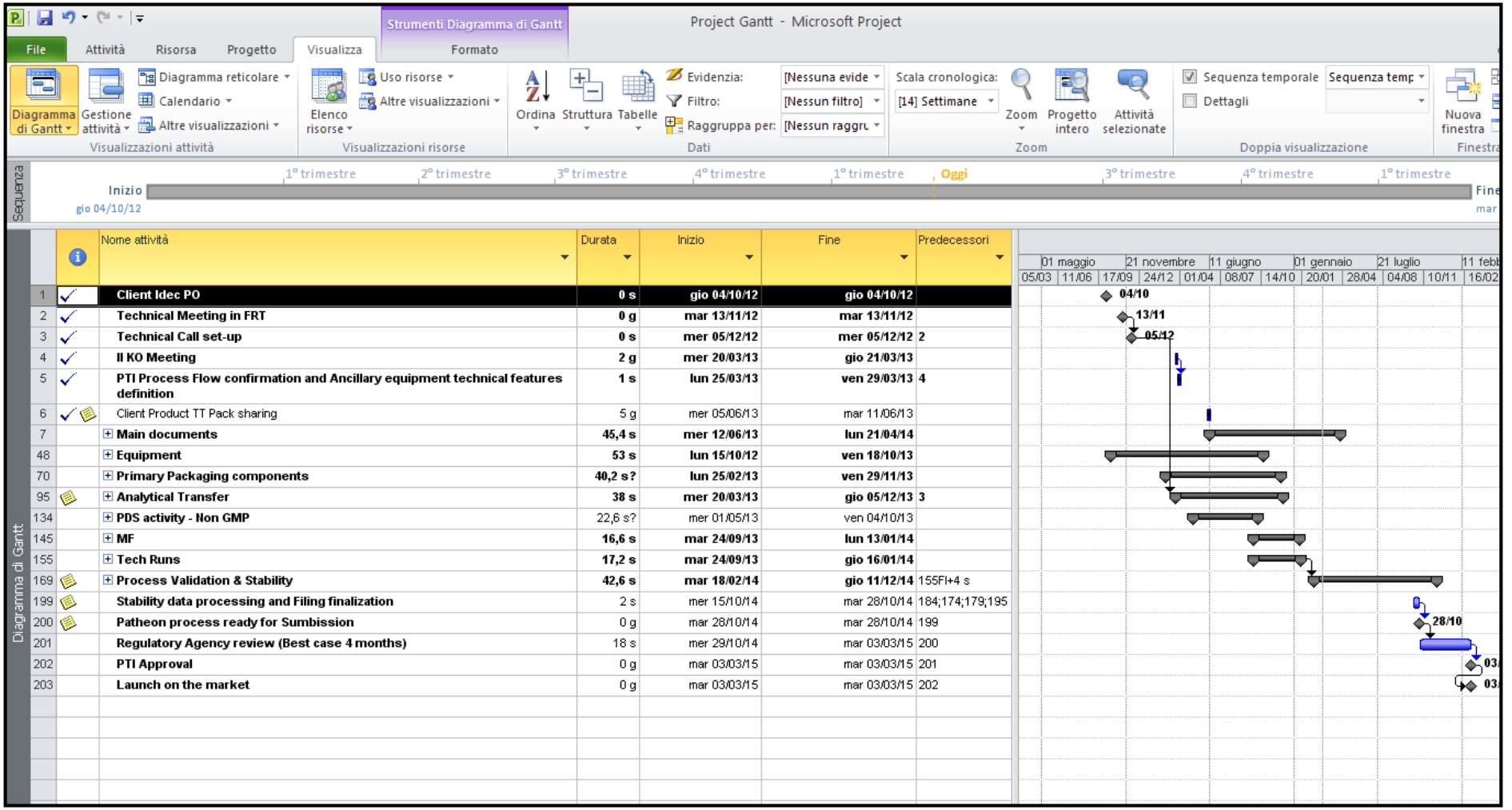


Pharma Tech Transfer Projects governance

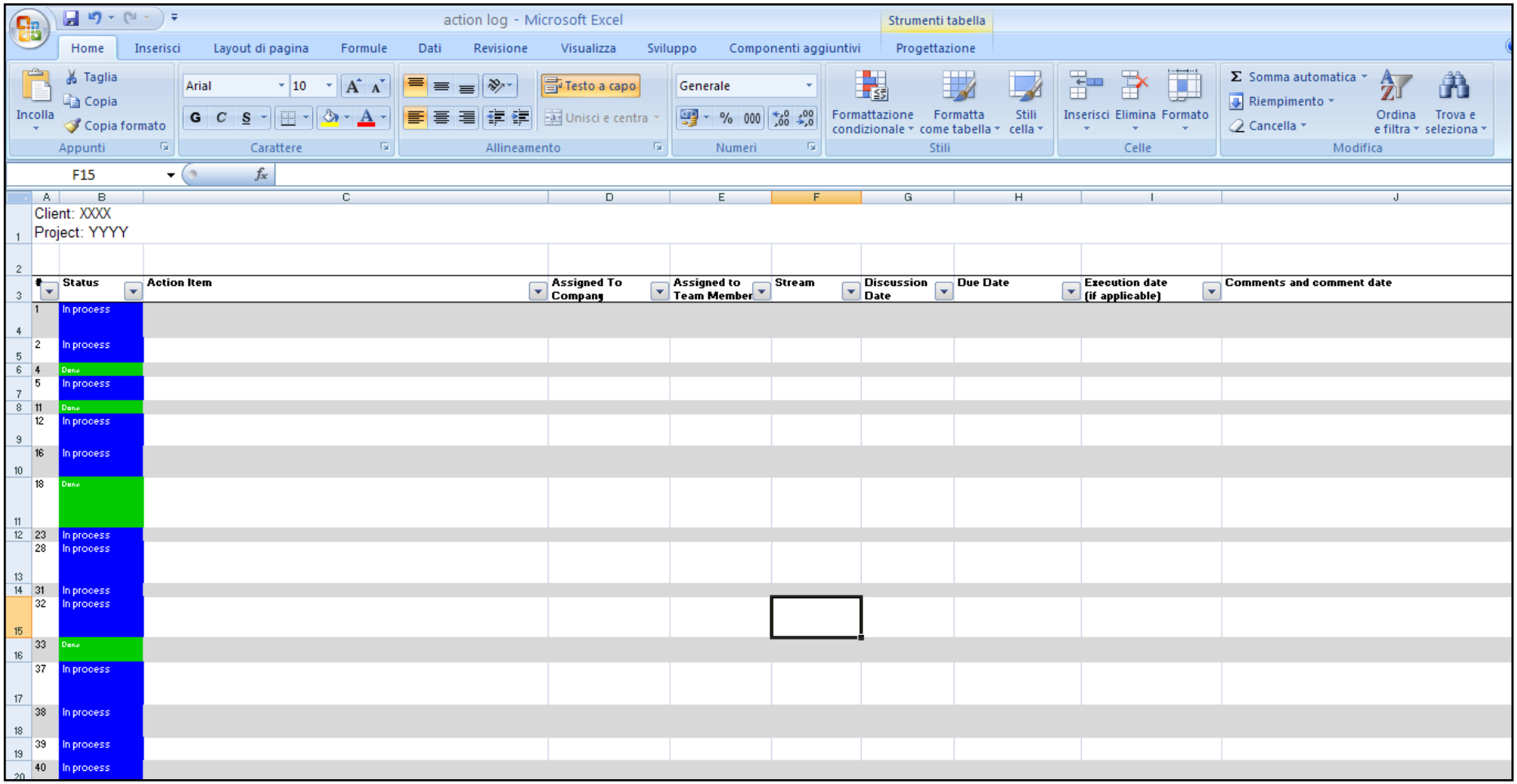
- Project Gantt
- Action List
- Decision List
- Risk Register
- Activities completion tracking

Define scope, plan, execute and track

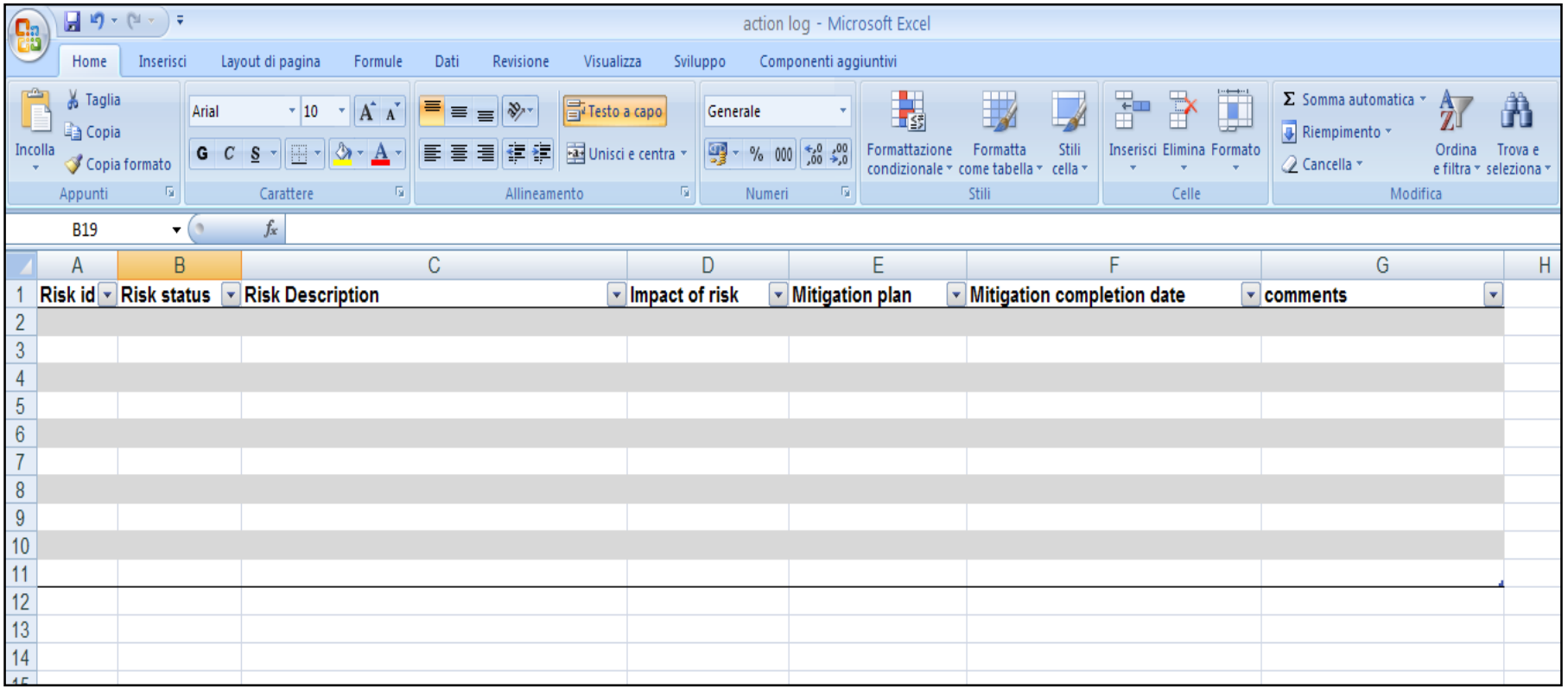
Pharma Tech Transfer Projects governance



Pharma Tech Transfer Projects governance



Pharma Tech Transfer Projects governance



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

Pharma Tech Transfer Projects governance

Docs/Info/Topic	YES	NO	N/A	Is there any disalignment/issue to be solved? (Y/N)	Action List (in case of gaps in column E)
1.0 Environmental Health & Safety					
1.1 Complete EHS Questionnaire					
1.2 MSDS for Drug Substance					
1.3 MSDS for Excipients					
1.4 Toxicity Data					
1.5 API exclusivity data (If Available)					
2.0 Materials					
2.1 Drug Substance					
2.1.1 Vendor Specification / CofA					
2.1.2 Sample of CofA, (Supplier/Client) including Bulk / Tap density and PSD data					
2.1.3 BSE/TSE Statement					
2.1.4 Residual Solvent Statement					
2.1.5 Letter Stating GMP status of manufacturer (if non-compendial)					
2.1.6 Import Routing Guide					
2.1.7 Memo to outline Micro Validation requirements or waiver					
2.1.8 Allergen letter (if applicable)					
2.1.9 API registration referential : CEP, DMF, scientific data)					
2.1.10 API Letter Stating Stability Data, including the requirement of templates during shipment.					
2.1.11 API supplier Audit report					
2.1.12 API supplier inspection					
2.1.13 API shipping container					
2.1.14 API packaging container (pictures)					
2.1.15 API critical handling information (e.i. light, moisture, oxygen, and/or heat sensitive, use of solvents)					
2.1.16 API shelf life					
2.1.17 API holding time, retest period					
2.2 Excipients					
2.2.1 Vendor Specification / CofA					
2.2.2 Sample of CofA (including bulk, tap density and PSD data)					
2.2.3 BSE/TSE Statement					
2.2.4 Residual Solvent Statement					
2.2.5 Letter Stating GMP status of manu					
2.1.6 Validated Test Methods (if non-co					
2.1.7 Memo to outline Micro Validation re					
2.1.8 Allergen letter (if applicable)					
2.3 Packaging Components					
2.3.1 Vendor Specification					

RACI Matrix

Role / Project Deliverable (or Activity)	Project Leadership – Sending Unit	Project Leadership – Receiving Unit	Project Leadership – Sponsor
. Project Assessment			
Preparation of the Tech Pack	R *(and A within the SU)*	A	
Analysis of the Tech Pack and confirmation of its appropriateness	I	R/A	
Sharing previous Project Gantt	R	A	
Previous lesson learnt sharing (process product management / Client management)	R	A	
Set up and handle an appropriate communication plan with SU	I	R/A	I
Set up and handle an appropriate communication plan with Client	I	R/A	C
Set up appropriate escalation process	I	R/A	C
Project Team and project governance definition	I	R/A	I
Client/Contract and CoS management		R/A	I
Set up an appropriate reporting process to upper management		R/A	C
. Project Planning			
Overall Technical Assessment preparation		R/A	
		A	
		R/A	
		A	
		R/A	I
		R/A	I
		A	
		R/A	
		A	

#	Meeting	Attendees	Frequency	Tentative Duration (min)	Purpose	Tool	Deliverables
1	Intra Company alignment	SU Leader RU Leader	Weekly/Biweekly based on project step	30	Alignment between Receiving Units and Sending Units in terms of evaluation/plans/actions	Project Dashboard	Meeting Minutes
2	Project Meeting	RU Leaders Client PM (or equivalent role)	Weekly	30	Discussion between PMs on Project status and execution, performance and communication between teams, main risks to be mitigated to avoid delay or stops	Project Dashboard Project Plan Risk Register	Meeting Minutes
3	Technical Meeting	RU Leader Client PM (or equivalent role) SMEs from parties based on agenda	Weekly	60	Detailed technical discussion on project tasks or issues	Technical Documents Project Plan Risk Register Project Dashboard	Meeting Minutes Risk Register updated Project Dashboard updated
4	Internal Sponsor meetings	SU Leader RU Leader Patheon Sponsor	Biweekly	30	Update the project sponsor on Project status , Client relationship, Patheon team performance and needs, risks and mitigation plan, issues and related action on going for resolution	Project Dashboard Risk Register	N/A
5	Project Sponsors Meetings	Patheon Sponsor Client Sponsor RU Leader Client PM (or equivalent role)	Monthly	30	Update the Client/Patheon Sponsors on the Project status, Relationship, Team performances, risks and needs	Project Dashboard Risk Register	Minutes

Pharma Tech Transfer Projects governance

Company Name

Projects KPI - Schedule Adherence

KPI in percentage %

Client	Product	Stage	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	TOTAL	Launch Date
		TT	N/A	100	N/A	0	25	0	N/A	N/A	N/A				25	March-17
		Registration	0	100	N/A	N/A	N/A	100	N/A	33	N/A				50	January-18
		TT	100	0	0	N/A	0	0	N/A	N/A	N/A				14	TBD
		TT	N/A	100	100	0	40	0	N/A	0	0				33	November-17
		Development	100	N/A	100	0	50	50	0	N/A	N/A				40	July-18
		TT	N/A	N/A	N/A	N/A	50	100	100	N/A	50				67	September-19
		TT	N/A	N/A	100	N/A	67	100	100	100	67				83	August-18
		Development	N/A	100	100	100	100	100	100	N/A	N/A				100	December-19
		TT	100	100	100	100	100	100	0	67	100				75	September-16
		TT	N/A	100	N/A	N/A	14	0	0	N/A	100				20	November-17
		TT	N/A	N/A	N/A	N/A	N/A	0	0	N/A	N/A				0	December-17
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				0	January-18
		TT	N/A	N/A	100	N/A	20	N/A	N/A	N/A	25				30	March-18
		Com - New API	N/A	100	100	N/A	N/A	N/A	N/A	100	100				100	Commercial
	Site Total		75	90	91	38	40	52	17	56	56				50	

Measurement	Color Code	Range
Red		Less Than 90%
Yellow		90% - 94%
Green		Over 95%

Pharma Tech Transfer Projects governance

Company Name

Projects KPI - Right the First Time (RFT)

KPI in percentage %

Client	Product	Stage	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	TOTAL
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		Com - New API	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		Registration	N/A	N/A	N/A	N/A	N/A	92	N/A	N/A	N/A				92
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		Development	100	N/A	N/A	N/A	N/A	100	N/A	N/A	N/A				100
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		Development	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		TT	N/A	N/A	N/A	N/A	N/A	0	N/A	N/A	100				0
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		TT	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A				N/A
		Com - New API	N/A	N/A	100	N/A	N/A	N/A	N/A	N/A	N/A				100
	Site Total		100	N/A	100	N/A	N/A	88	N/A	N/A	100				90

Measurement	Color Code	Range
Red		Less Than 90%
Yellow		90% - 94%
Green		Over 95%

Pharma Tech Transfer Projects governance

Human Beings, who are almost unique in having the ability to learn from the experience of others are also remarkable for their apparent disinclination to do so..

Douglas Adams

Pharma Tech Transfer Projects governance

What is lesson learned…terminology to identify actions or activities related to the act of ***learning from experience to obtain improvements of the current way of working.***

Idea and main concept behind the definition…using a robust, structured and formal process team can reduce risk of doing same mistakes and increase success rate of their projects

LL circle: Data Collection – Data Analysis – Action Plan definition – Plan Execution

- Data collection : Collect data, facts, from previous projects/TT
- Data Analysis : Analyze data to confirm event, measure severity and prevention rate
- Action Plan definition: Define improvements to the existing procedure or ways of working
- Plan execution: Execute plan changing internal procedure and adopting appropriate communication plan

Lesson Learned Capability: need to be established, trained and improved step by step.

Pharma Tech Transfer Projects Risk Management

What does RM mean in TT?

Technology Transfer – Risk Management

- **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.

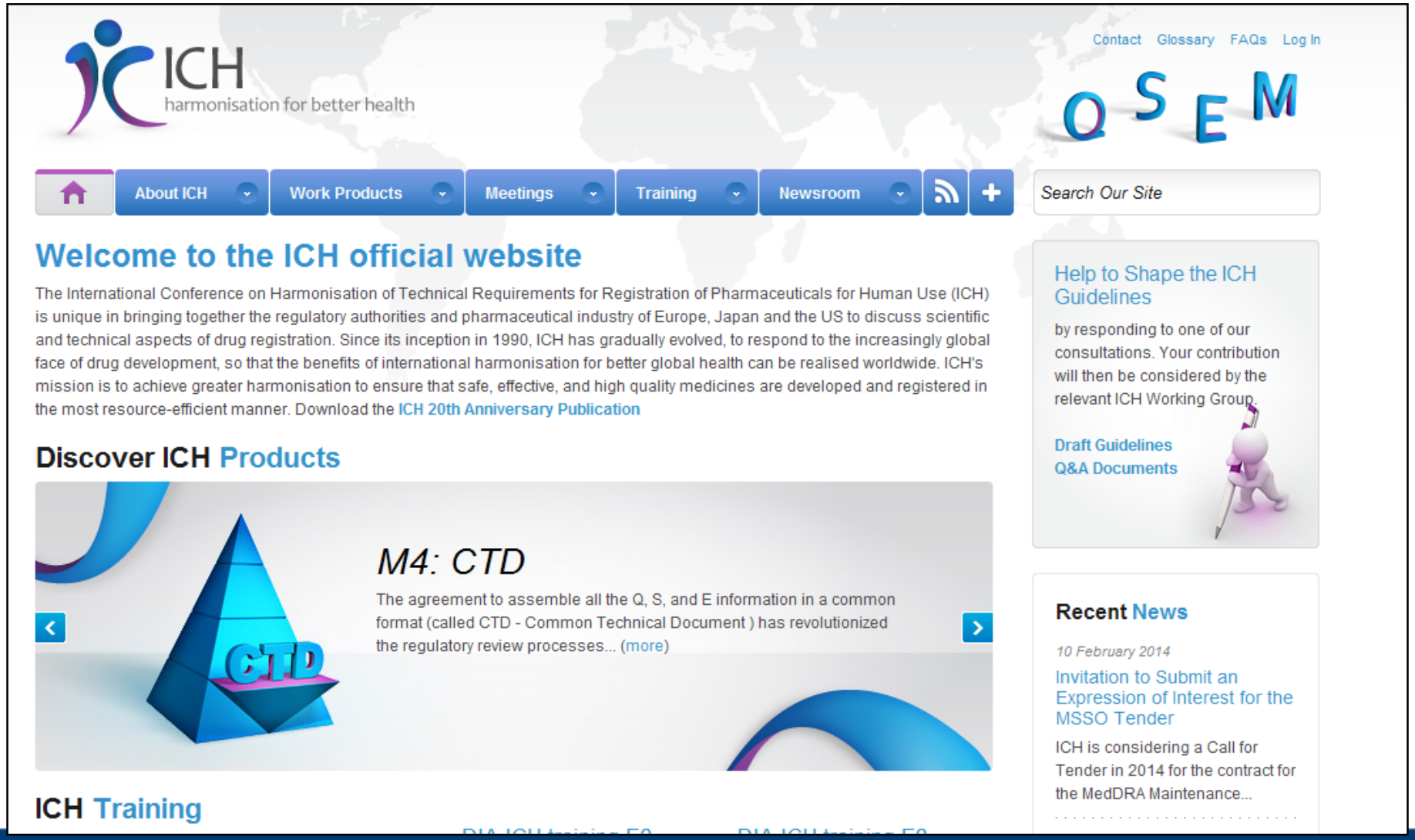
- **Risk acceptance**

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

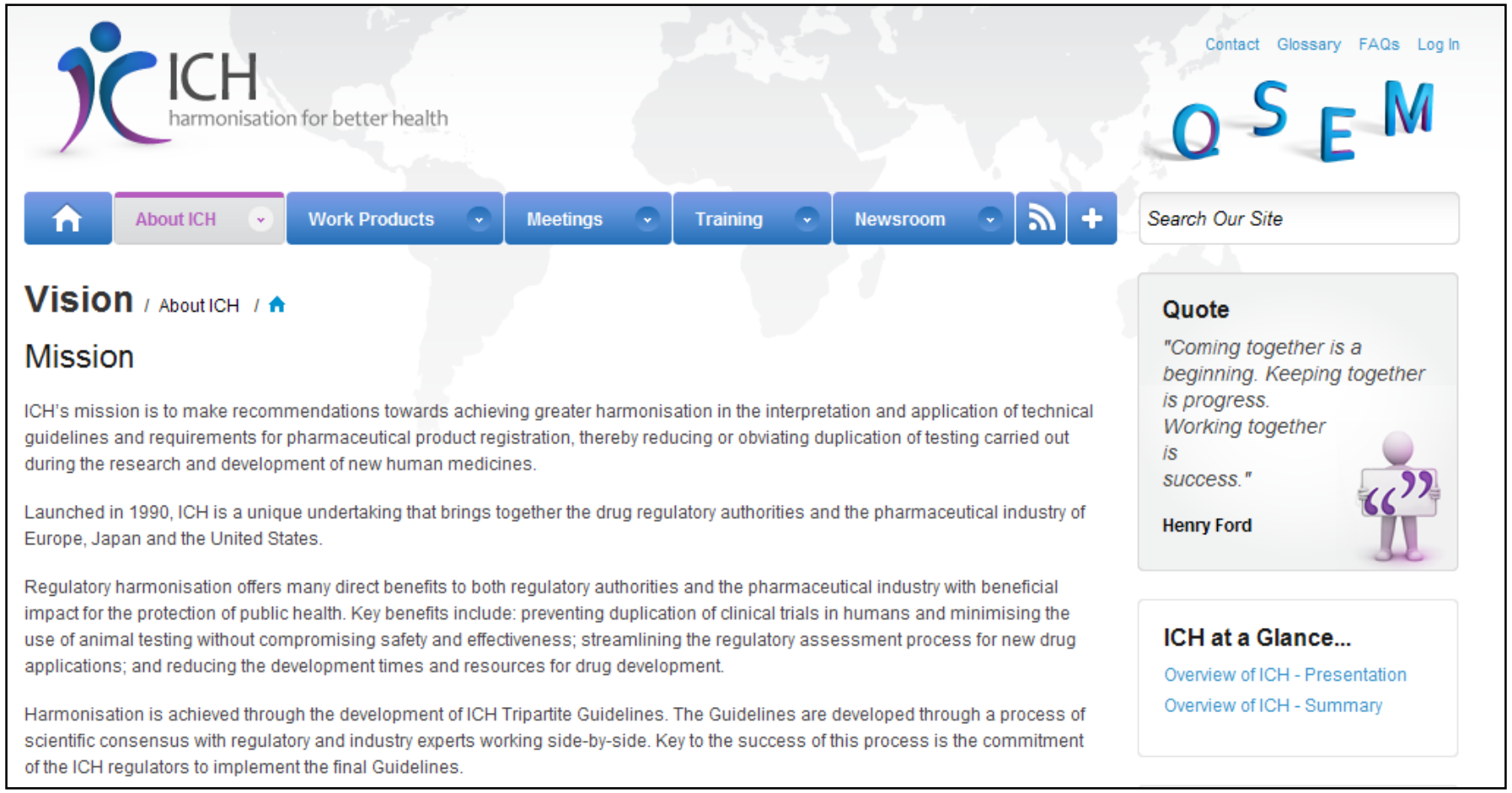
- **Risk communication**

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

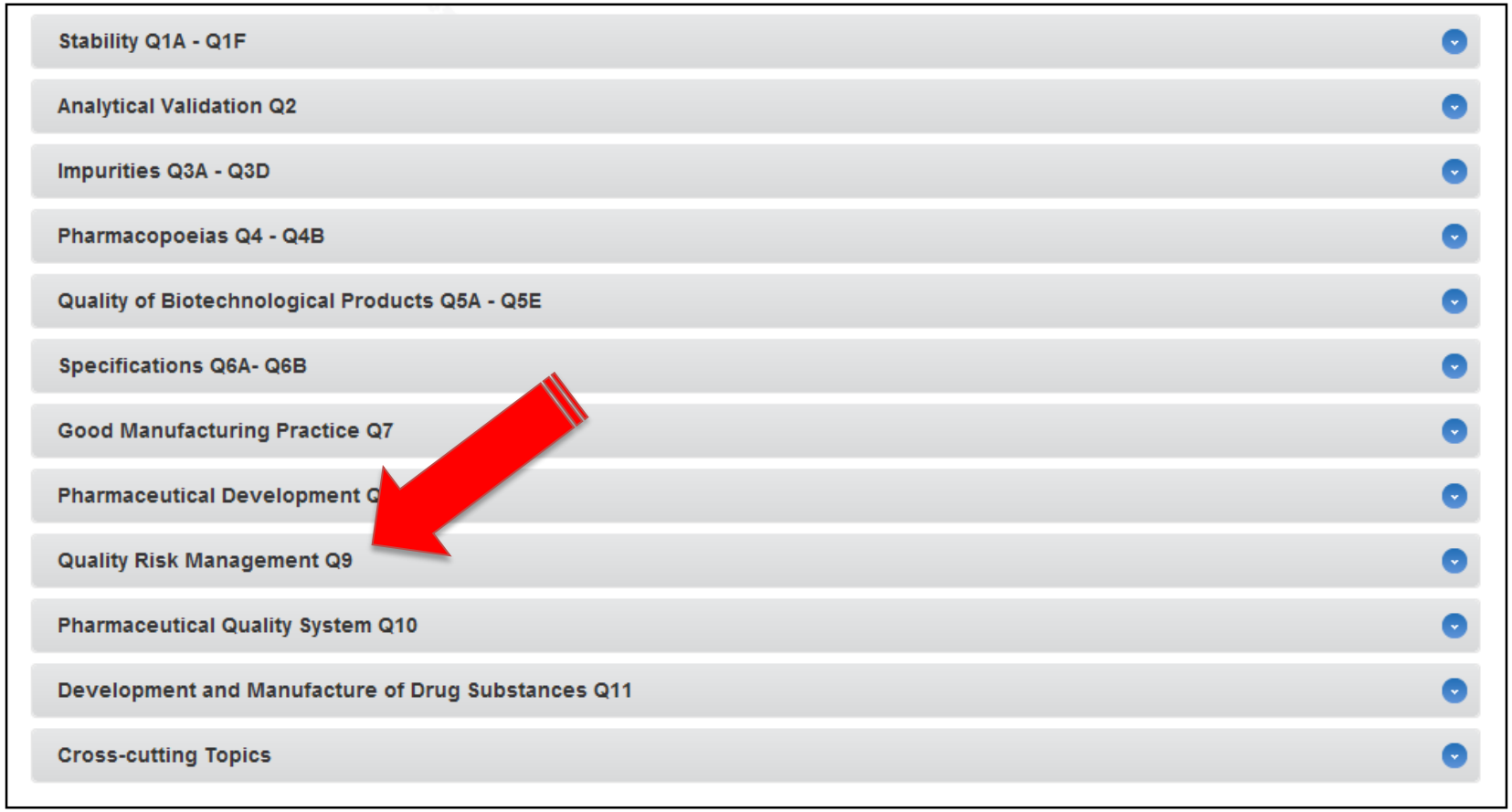
ICH & Risk - http://www.ich.org/



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



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



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

- 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.

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

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.

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

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.

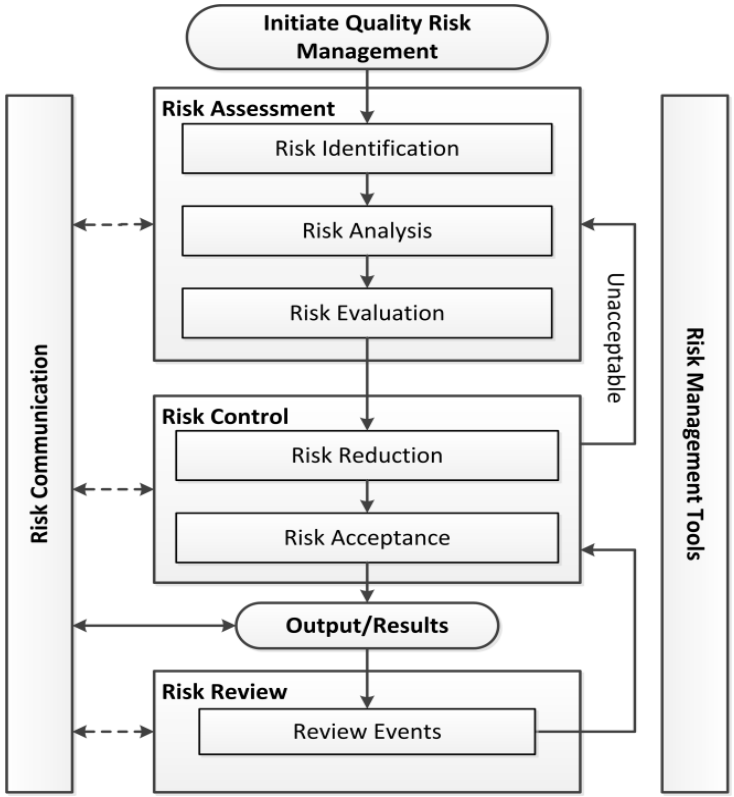
Decision makers should

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

• ensure that a quality risk management

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

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.”



Technology Transfer – Risk Management

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

Technology Transfer – Risk Management

- 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

Technology Transfer – Risk Management

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

Technology Transfer – Risk Management

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)

Technology Transfer – Risk Management

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

Technology Transfer – Risk Management

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

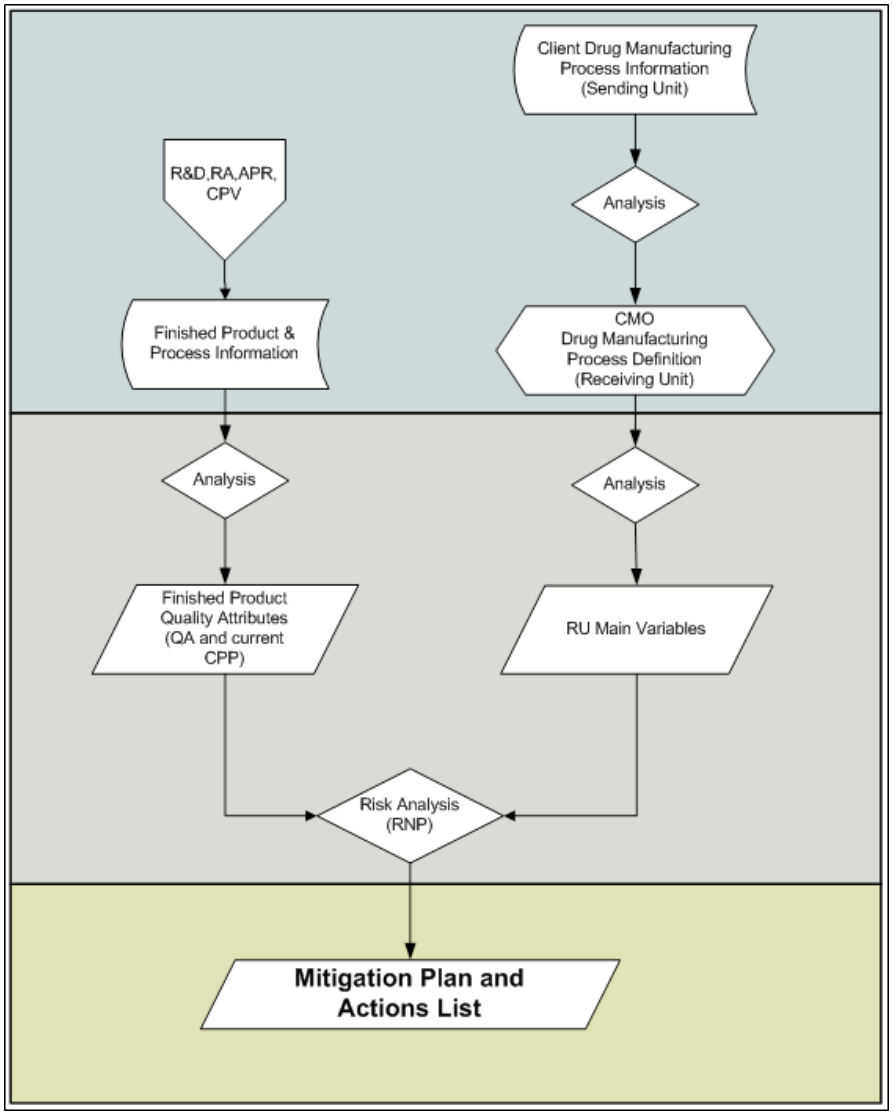
Technology Transfer – Risk Management

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

Technology Transfer RA Approach



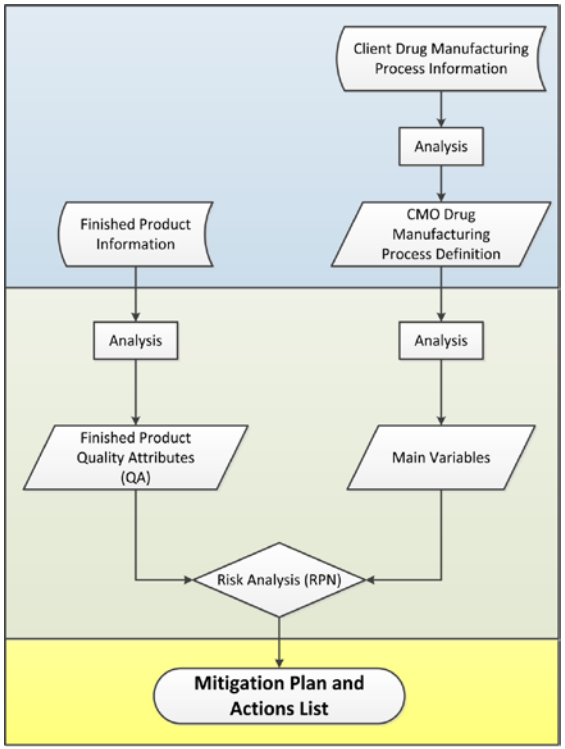
Data collection

Data evaluation

Data use

Technology Transfer RA Approach

Our Risk Assessment and Mitigation approach is based on several Source of information, linked to create a TT Starting Story



Source 1 – Definition of the Main Process Variables of the product (SU -> RU) *(examples below)*

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

Source 2 – Definition of the Quality Attributes (RU) *(examples below)*

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

Technology Transfer RA Approach

Risk Assessment and Mitigation Approach:

- is part of part of Company DNA, therefore application is a must for all our TTs and during the whole project lifecycle;
- Has to be in line with the current regulatory guidance, GMP and based on scientific sound
- Has to be managed by appropriate flexible, robust and efficient tools
- Is a multifactorial exercise that takes in considerations internal and external variables of the project/process/product/lines
- Provides a clear path forward starting with QbD and development (where necessary) and ending with a reproducible, efficient and in quality market supply

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 same stoppers will be used to guarantee no anomalous interaction with stopper coating and rubber. Stability data were collected by the SU; no interaction issues were reported to RU.
			The coating material can modify the chemical solution profile	3	2	3	18	
		Appearance	Substances released from the stopper or from the coating can induce flocculation or coagulation events in the solution	3	2	1	6	
			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.

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. Mixing studies will be agreed with the SU and performed during the engineering batch. 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
		Osmolality	Dissolution speed insufficient for complete dissolution and an homogenous system	3	3	1	9	
		Appearance	Mixing system not appropriate to guarantee uniform batch mixing	3	3	3	27	
		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 2 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.

Technology Transfer RA Approach

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 and compounding	pH	Dissolution speed is insufficient for complete dissolution and a homogenous system.	3	3	1	9	During the performance qualification, the mixing device of the tank used in the RU will be challenged. Mixing studies will be agreed on by the SU and performed during the engineering batch.
		Osmolality	Dissolution speed is insufficient for complete dissolution and a homogenous system.	3	3	1	9	
		Appearance	Mixing system is 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 is outside the 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 can affect the analysis	3	2	2	12	The sampling system will be made of pharmaceutical-grade glass. The SU has collected data on compatibility, and the solution is declared compatible with glass devices.
		Sterility	Preparation time can affect the 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	Particles release from disposable hoses may impact the particulate matter profile	3	2	3	18	Use Silicon, platinum-cured, disposable hose certified for pharmaceutical use for solution transfer. To address particle release from the hoses used in grade C, filter the solution three 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.
			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.

Technology Transfer – Take Away from PDA TT IG

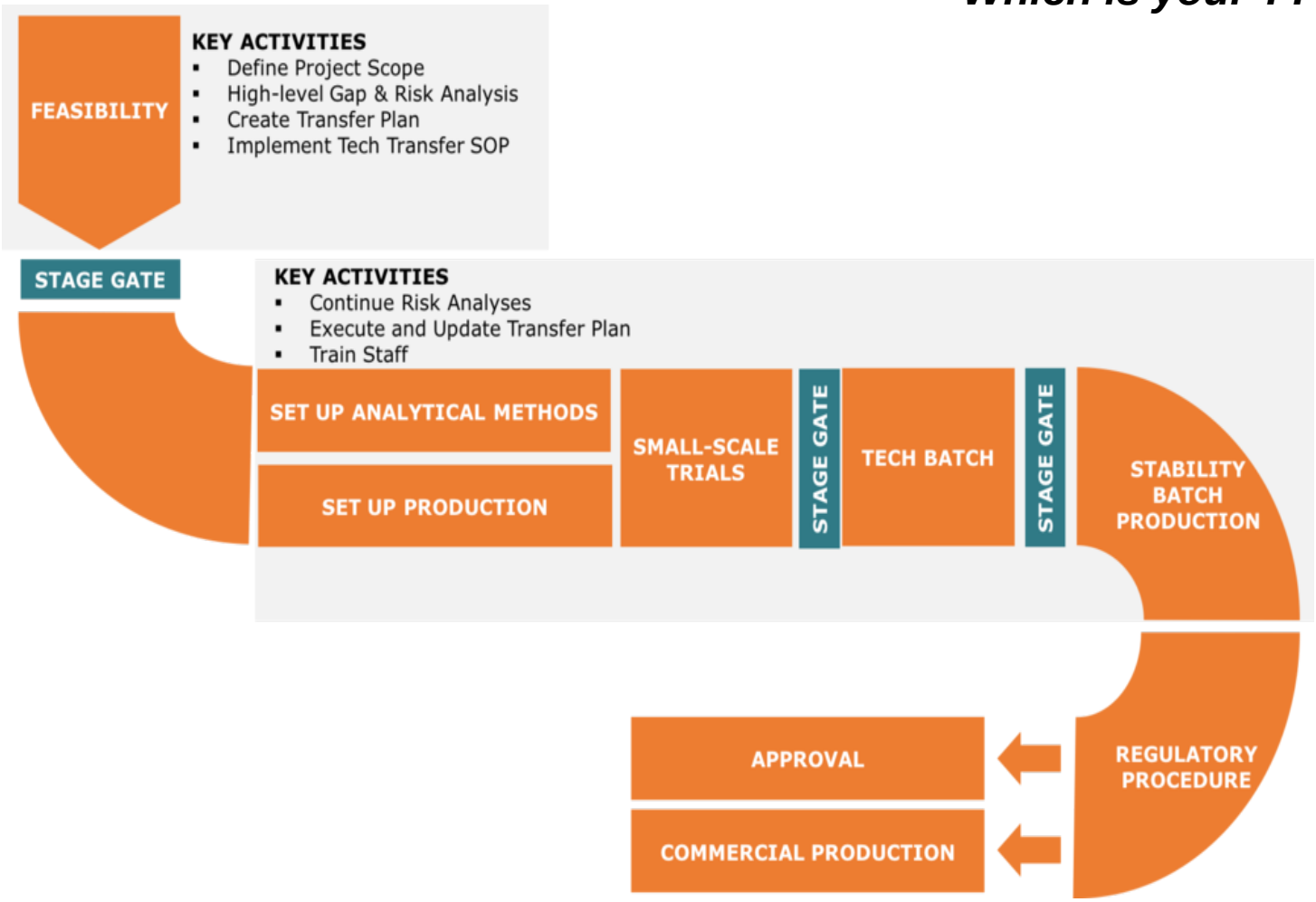
Technology Transfer

Key factors for success no matter which kind of TT we are considering

- Sending unit and receiving unit work closely with each other.
- Clear understanding of roles and responsibilities of both sending unit and receiving unit team members.
- Complete technology transfer package.
- Quality Risk Management.
- Effective knowledge transfer and training.
- Stage Gate Approach

Technology Transfer

Which is your TT RoadMap?



PDA TT IG Survey

1. Which is the main difficulty during a Development to Clinical phase TT?

Lack of information regarding robustness of process

2. Which is the main difficulty during a Clinical Phase to Commercial TT?

Appropriateness of batch scale based on market demand

3. Which is the main difficulty during a Commercial to Commercial TT?

MSA negotiation and agreement (in case of external TT)

R&R between sites (in case of internal TT)