Sept 2022, Angela Molaschi

Managing Technology Transfer Projects in Pharma

PDA
Parenteral Drug Association

CONNECTING
PEOPLE
SCIENCE AND
REGULATION®

PDA

About us

- **The Parenteral Drug Association (PDA)** is the leading global provider of science, technology and regulatory information and education for the pharmaceutical and biopharmaceutical community.

- Founded in 1946 is a not profit organization.

- PDA commitment is to developing **scientifically sound, practical technical information and resources to advance science and regulation** through the expertise of its more than 9500 members worldwide.
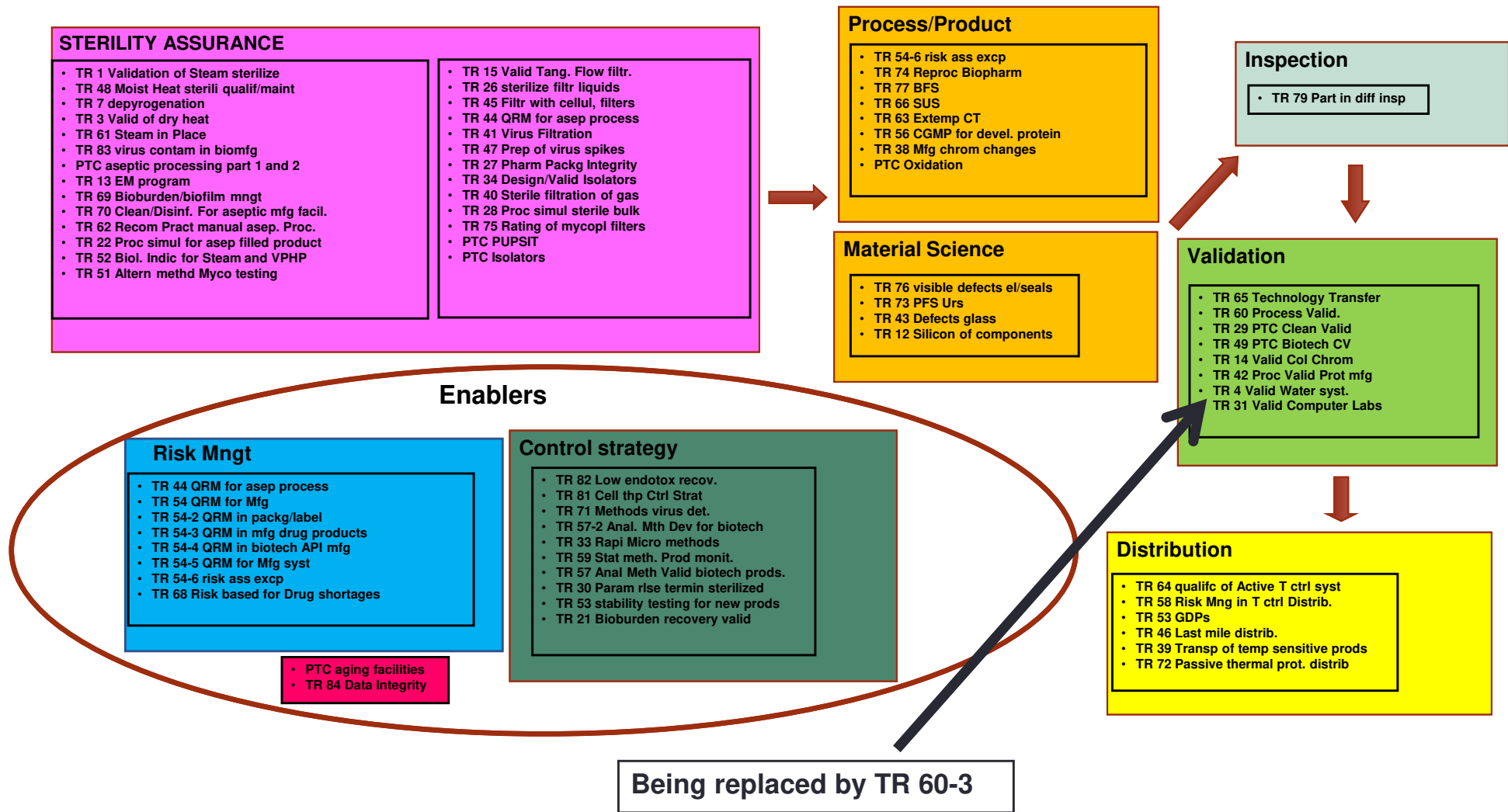
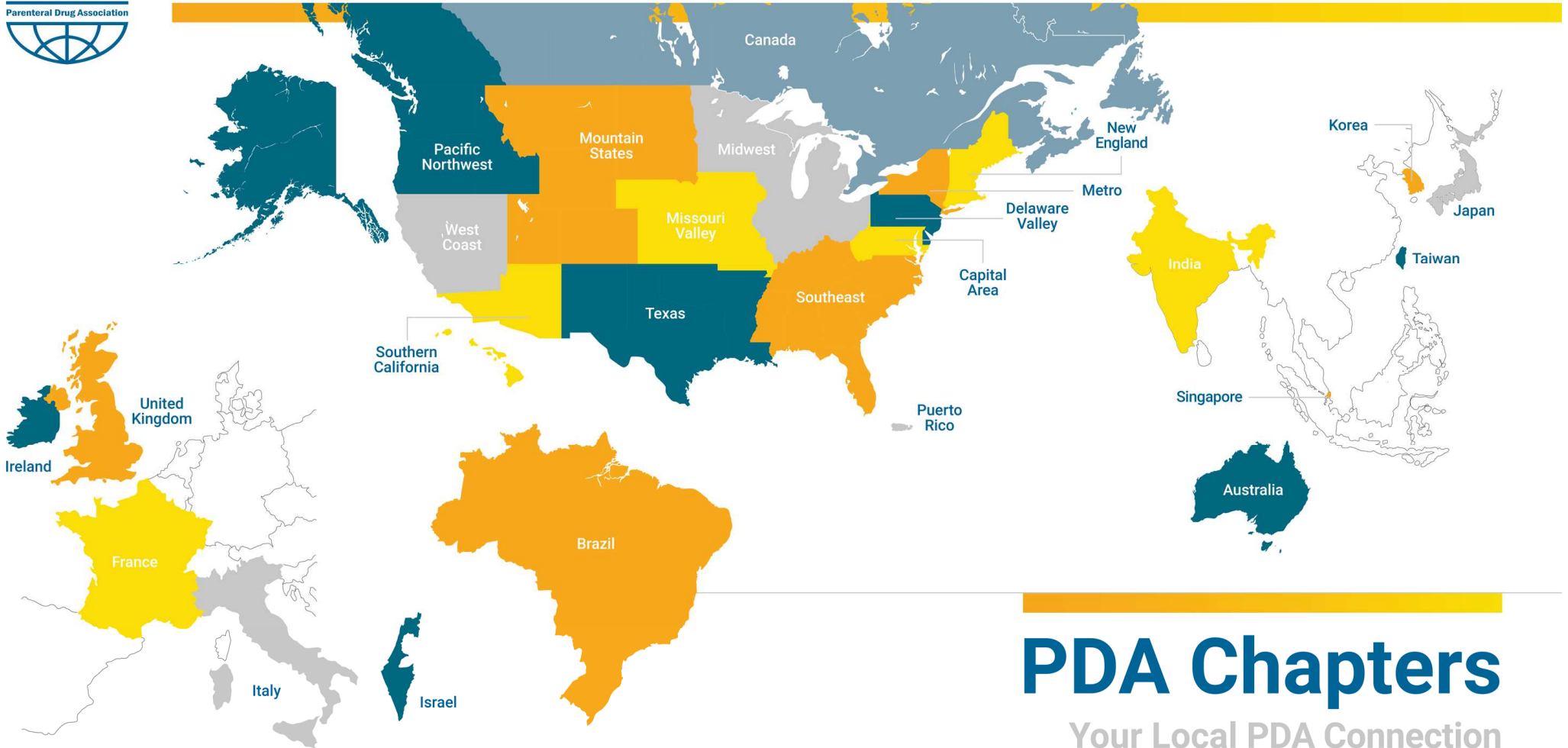Our mission:
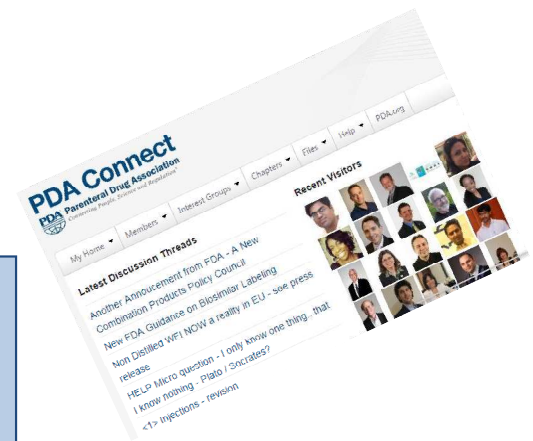
« Connecting People, Science and Regulation»

- PDA is based on 4 main boards, each overseeing Interest Groups covering specific topics. See link

- [Technical Advisory Boards | Parenteral Drug Association (pda.org)](pda.org)

  - BioManufacturing Advisory Board (e.g. Vaccines, Fermentation, etc..)

  - Regulatory and Quality Advisory Board (Inspection Trends, Quality Risk Mngt, etc..)

  - Scientific Advisory Board (e.g. Process Validation, Visual Inspection, etc..)

  - Advanced Therapy Medicinal Products (ATMP)

- At geographical level, PDA is based on Chapters: there are 14 US Chapters, 4 European Chapters (France, Italy, Ireland, UK), Israel Chapter, 1 Chapter in Latin America and 6 chapters in Asia Pacific. See link

- [PDA Chapters | Pharmaceutical Manufacturing Association]()

Connecting People, Science and Regulation®

PDA technical reports

STERILITY ASSURANCE

- TR 1 Validation of Steam sterilize
- TR 48 Moist Heat sterili qualif/maint
- TR 7 depyrogenation
- TR 3 Valid of dry heat
- TR 61 Steam in Place
- TR 83 virus contam in biomfg
- PTC aseptic processing part 1 and 2
- TR 13 EM program
- TR 69 Bioburden/biofilm mngt
- TR 70 Clean/Disinf. For aseptic mfg facil.
- TR 62 Recom Pract manual asep. Proc.
- TR 22 Proc simul for asep filled product
- TR 52 Biol. Indic for Steam and VPHP
- TR 51 Altern methd Myco testing

- TR 15 Valid Tang. Flow filtr.
- TR 26 sterilize filtr liquids
- TR 45 Filtr with cellul, filters
- TR 44 QRM for asep process
- TR 41 Virus Filtration
- TR 47 Prep of virus spikes
- TR 27 Pharm Packg Integrity
- TR 34 Design/Valid Isolators
- TR 40 Sterile filtration of gas
- TR 28 Proc simul sterile bulk
- TR 75 Rating of mycopl filters
- PTC PUPSIT
- PTC Isolators

Process/Product

- TR 54-6 risk ass excp
- TR 74 Reproc Biopharm
- TR 77 BFS
- TR 66 SUS
- TR 63 Extemp CT
- TR 56 CGMP for devel. protein
- TR 38 Mfg chrom changes
- PTC Oxidation

Material Science

- TR 76 visible defects el/seals
- TR 73 PFS Urs
- TR 43 Defects glass
- TR 12 Silicon of components

Inspection

- TR 79 Part in diff insp

Validation

- TR 65 Technology Transfer
- TR 60 Process Valid.
- TR 29 PTC Clean Valid
- TR 49 PTC Biotech CV
- TR 14 Valid Col Chrom
- TR 42 Proc Valid Prot mfg
- TR 4 Valid Water syst.
- TR 31 Valid Computer Labs

Enablers

Risk Mngt

- TR 44 QRM for asep process
- TR 54 QRM for Mfg
- TR 54-2 QRM in packg/label
- TR 54-3 QRM in mfg drug products
- TR 54-4 QRM in biotech API mfg
- TR 54-5 QRM for Mfg syst
- TR 54-6 risk ass excp
- TR 68 Risk based for Drug shortages

- PTC aging facilities
- TR 84 Data Integrity

Control strategy

- TR 82 Low endotox recov.
- TR 81 Cell thp Ctrl Strat
- TR 71 Methods virus det.
- TR 57-2 Anal. Mth Dev for biotech
- TR 33 Rapi Micro methods
- TR 59 Stat meth. Prod monit.
- TR 57 Anal Meth Valid biotech prods.
- TR 30 Param rlse termin sterilized
- TR 53 stability testing for new prods
- TR 21 Bioburden recovery valid

Distribution

- TR 64 qualifc of Active T ctrl syst
- TR 58 Risk Mng in T ctrl Distrib.
- TR 53 GDPs
- TR 46 Last mile distrib.
- TR 39 Transp of temp sensitive prods
- TR 72 Passive thermal prot. distrib

Being replaced by TR 60-3

PDA Chapters

Your Local PDA Connection

About the Interest Groups

About the Interest Groups

Connecting People, Science and Regulation®

Introduction

Why we are here?

pda.org

Why join this training?
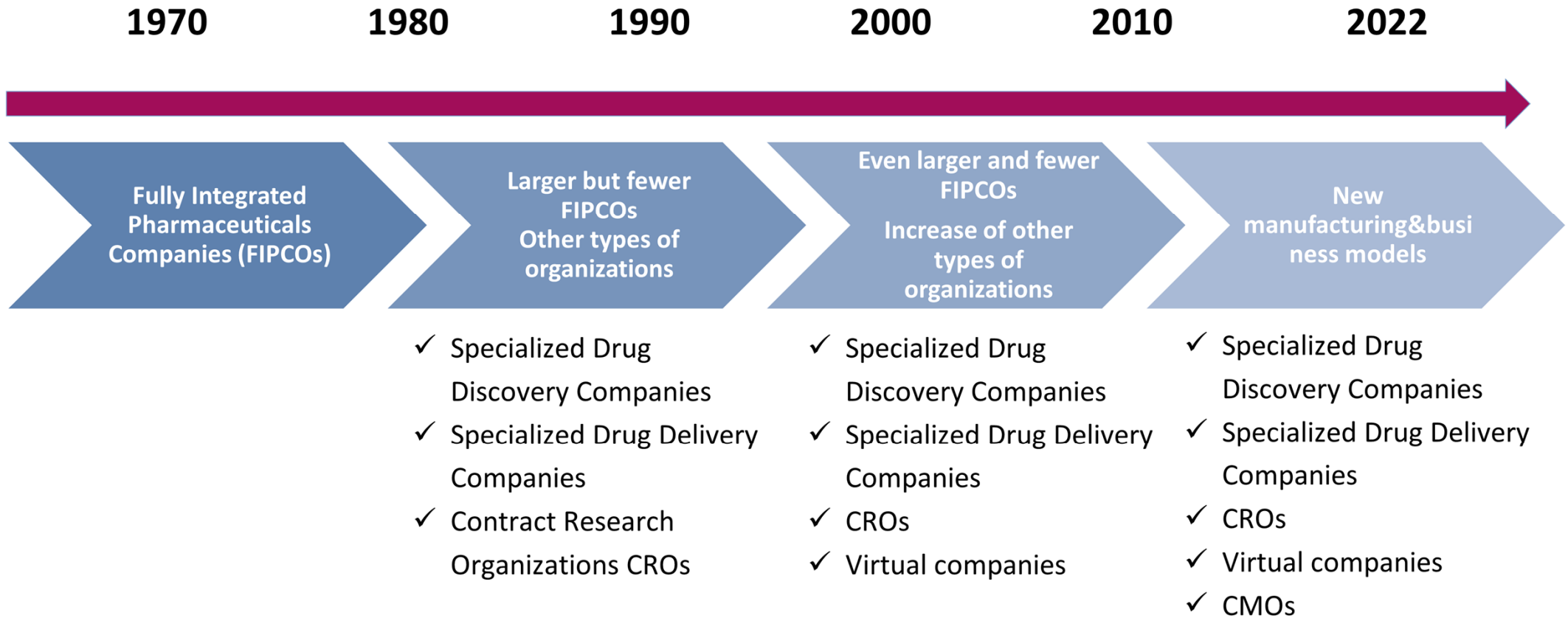
$1T

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

Connecting People, Science and Regulation®

Pharmaceutical world evolution

1970	1980	1990	2000	2010	2022

Fully Integrated Pharmaceuticals Companies (FIPCOs)

**Larger but fewer FIPCOs
Other types of organizations**

**Even larger and fewer FIPCOs
Increase of other types of organizations**

New manufacturing&business models

✓ Specialized Drug Discovery Companies
✓ Specialized Drug Delivery Companies
✓ Contract Research Organizations CROs

✓ Specialized Drug Discovery Companies
✓ Specialized Drug Delivery Companies
✓ CROs
✓ Virtual companies

✓ Specialized Drug Discovery Companies
✓ Specialized Drug Delivery Companies
✓ CROs
✓ Virtual companies
✓ CMOs

- Patents expirations and generic drugs

- Globalization

- Mergeries and aquisitions

- Huge increase of the development and registration costs

- More stringent and demanding regulatory requirements

- Competition:

    - Outsourcing increase

    - New markets and new competitors

    - New business models

.......all that and much more led to the evolution of the **Pharma world and models**

- Increase of complexity and competition
- Different and new business models (i.e. equity funds)
- Outsourcing increase: CDMO model
- Production sites rationalization
- High specialization
- Hig value products VS medium/low value products
- Importance of the costs
- ….last but not least covid impact:
    - Big growth in vaccines sector
    - Big growth of CDMO model
    - Stable business in life-saving products
    - Impact on non life-saving products (need of conversion)
    - Priority investment in some areas

- Born in Fully Integrated Pharmaceuticals Companies (FIPCOs) as transfer/scale up from development to production/industrial scale

- Usually within the same site

- Managed by R&D

- High specialization and technical expertise of who is managing and executing TT

- Very specific activity

- High budget and resources

- Long timelines
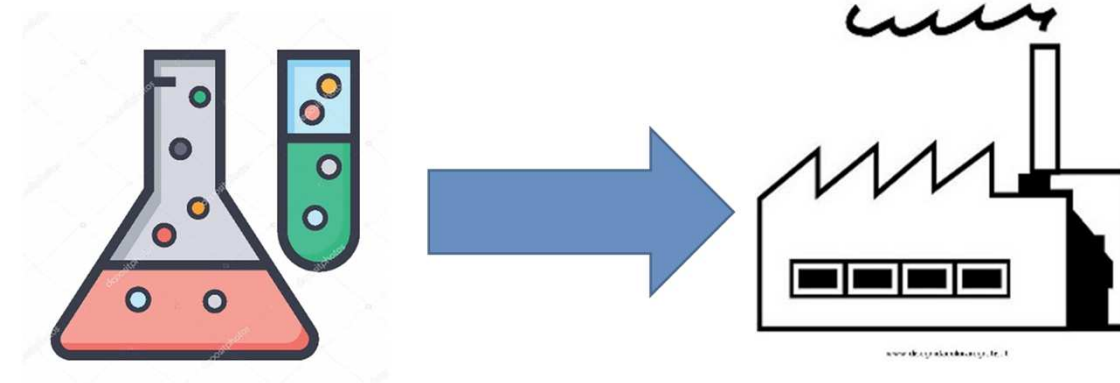
With the pharmaceutical world evolution Technology Transfer has become:

- More frequent and with increased values (acquistions, mergeries, new strategies, outsourcing, shorter products life..)

- More international

- More complex (different sites, different cultures, different procedures, different technologies and equipment)

- A fundamental part of pharmaceutical processes

- Globally recognized in the pharmaceutical business: Technology Transfer dedicated functions

- In the complex and fast pharmaceutical business the development and technology transfer of rubust formulations and processes is «critical»

- Due to high differentiation of current pharmaceutical business different Technology Transfer types were born

- All the main Pharma companies have created their own technology transfers models and culture

- Big pharma (brand)
- R&D and production in the same site
- R&D focus
- High technical skills
- Focus tecnico
- High budget

- Big pharma (brand)
- Generic market
- Development centralization
- R&D and production in different sites
- TT Manager/PM
- Growing importance of management and relationships

- Outsourcing
- CMOs business
- TT among different sites and companies
- Higher organization and management activities
- Less technical
- Higher attention on costs

- CMOs business
- New products and technologies (biologics, biosmililars)
- TT among different sites and companies
- Different TT types

- CMOs business
- New business and companies types
- High importance of the contractual part
- Focus on budget and costs

Internal development /intracompany primary TTs	External development /intraintercompany primary TTs)	Secondary TTs (full process)	Secondary TT (partial process)	Outsourcing

'70/'80 → **Now**

Why join this training?

PDA ®
Parenteral Drug Association

$1T

Global Rx sales by 2020

$160B

Global pharma and biotech R&D spend by 2020

60 to 10

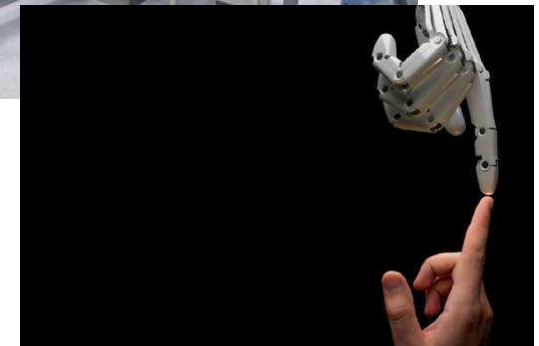Shrink in number of Pharma players due to M&A in the last 20 years

TT IS AND WILL BECOME A MORE CRITICAL BUSINESS NEED, A "BEST TO BEST DEAL" WITH CUSTOMERS, TOP PLAYERS LOOKING FOR CDMO TOP PLAYERS
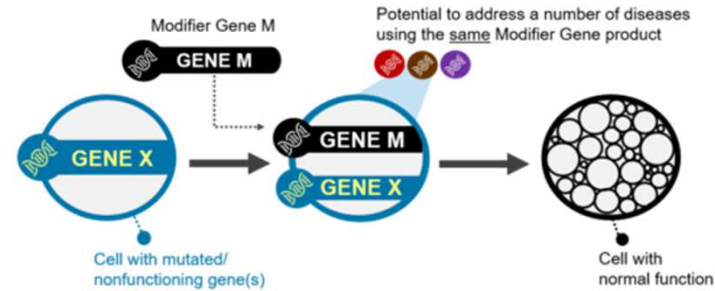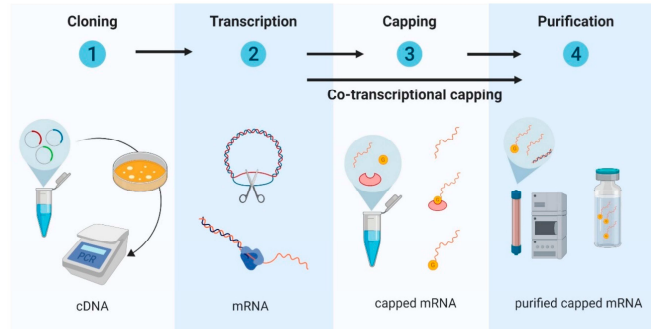
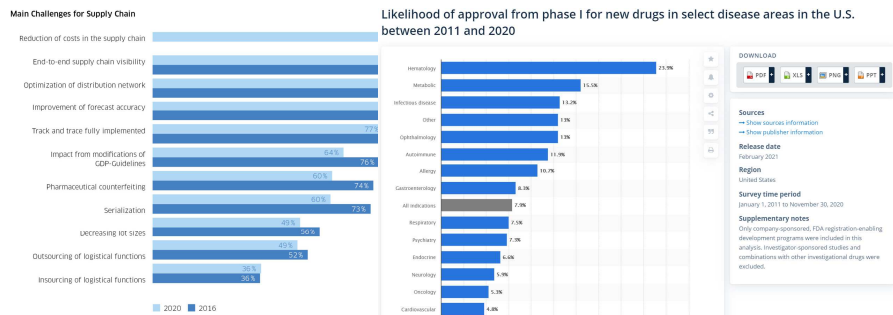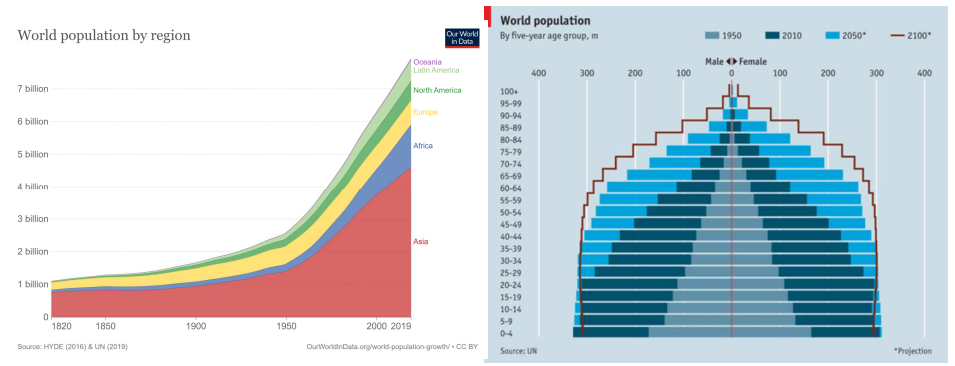**EVEN MORE TRUE, BASED ON PHARMA INDUSTRY DICHOTOMY PLANNED AS FUTURE SCENARIO**

&

NEW PLATFORMS COMING UP WITH NEEDS OF QUICK AND CONSISTENT SCALE UP


OPTIMIZATION PRESSURE IN PHARMA

CAPACITY NEEDED FOR DRUG SUPPLY TO PEOPLE DUE TO EPIDEMIOLOGY AND DEMOGRAPHY TRENDS

- **PATIENTS DIFFULTIES TO GET MEDICINES**

  - SUPPLY CHAIN DISRUPTION

  - LOW CAPACITY AVAILABLE FOR A CERTAIN MANUFACTURING

  - DELAY IN NEW DRUG APPROVAL AND DISTRIBUTION

  - DELAY IN CLINICAL STAGE

  - DELAY IN NEW DRUG DEVELOPMENT

PDA ®
Parenteral Drug Association
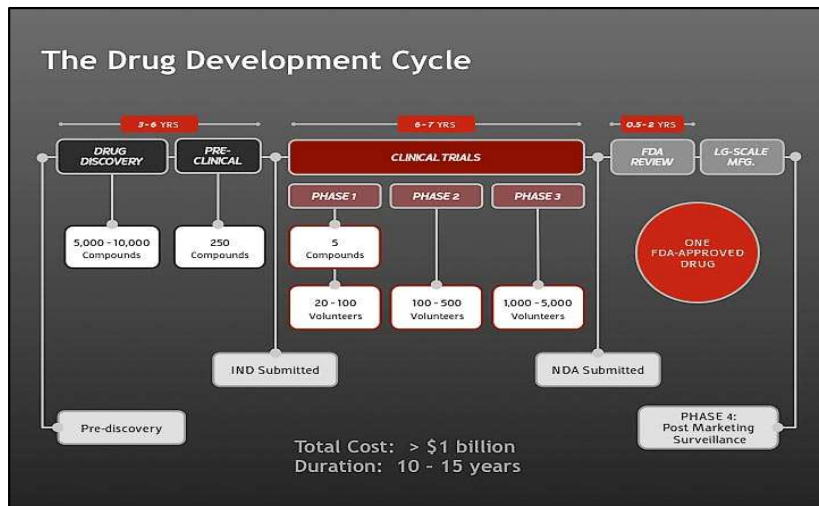
- Incredible **increase** of number of **Technology Transfer projects** (TTP) in the pharmaceutical environment, both internal & external and consequent increase of attention on Technology Transfer (TT) handling by Authorities;
- **Business Opportunity** for big and small companies
- Project **complexity** is growing TT Experts have to be prepared to face challenges
- **Dynamic and challenge** environment

KEEP CALM AND HAVE FUN

KeepCalmAndPosters.com

Connecting People, Science and Regulation®

PDA and Technology Transfer group

- 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, vs 02 issued in June 2022

- 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

SUCCESS ROADMAP

My expectations for the two days…

- Share experience on TT

- Benchmarking on TT organization, Approaches

- Understand opportunity for improvements

- Discuss challenges and practical cases

- Learn from each other experience

- Networking

Connecting People, Science and Regulation®

Tell Me About Yourself

What is your expectation?

Connecting People, Science and Regulation®

Technology Transfer in Pharma: main concepts

What is a Technology Transfer?

pda.org

What is Technology Transfer?

Connecting People, Science and Regulation®

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)

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).

Sending unit

Receiving unit

PDA – PMCO Program – Technical Report N.65

PDA
Parenteral Drug Association

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** is a systematic procedure that shall be executed with the aim to transfer knowledge and experience related to a pharmaceutical process from one organization to another. Technology transfer includes documentation transfer and proven ability of the receiving unit to execute what has been transferred»

«Technology Transfer is a learning and growing experience for both the units involved»

31

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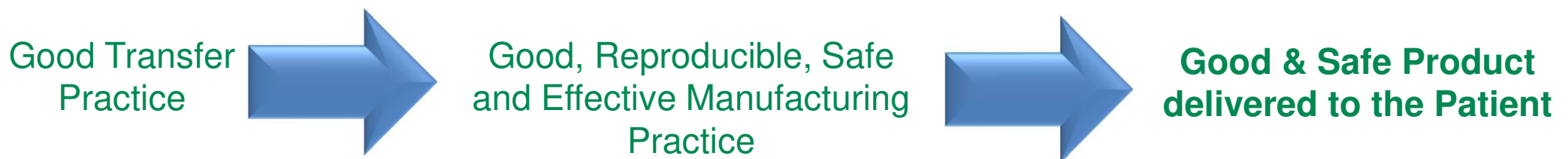
Good Transfer Practice → Good, Reproducible, Safe and Effective Manufacturing Practice → **Good & Safe Product delivered to the Patient**

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

- Are managed by a team

33

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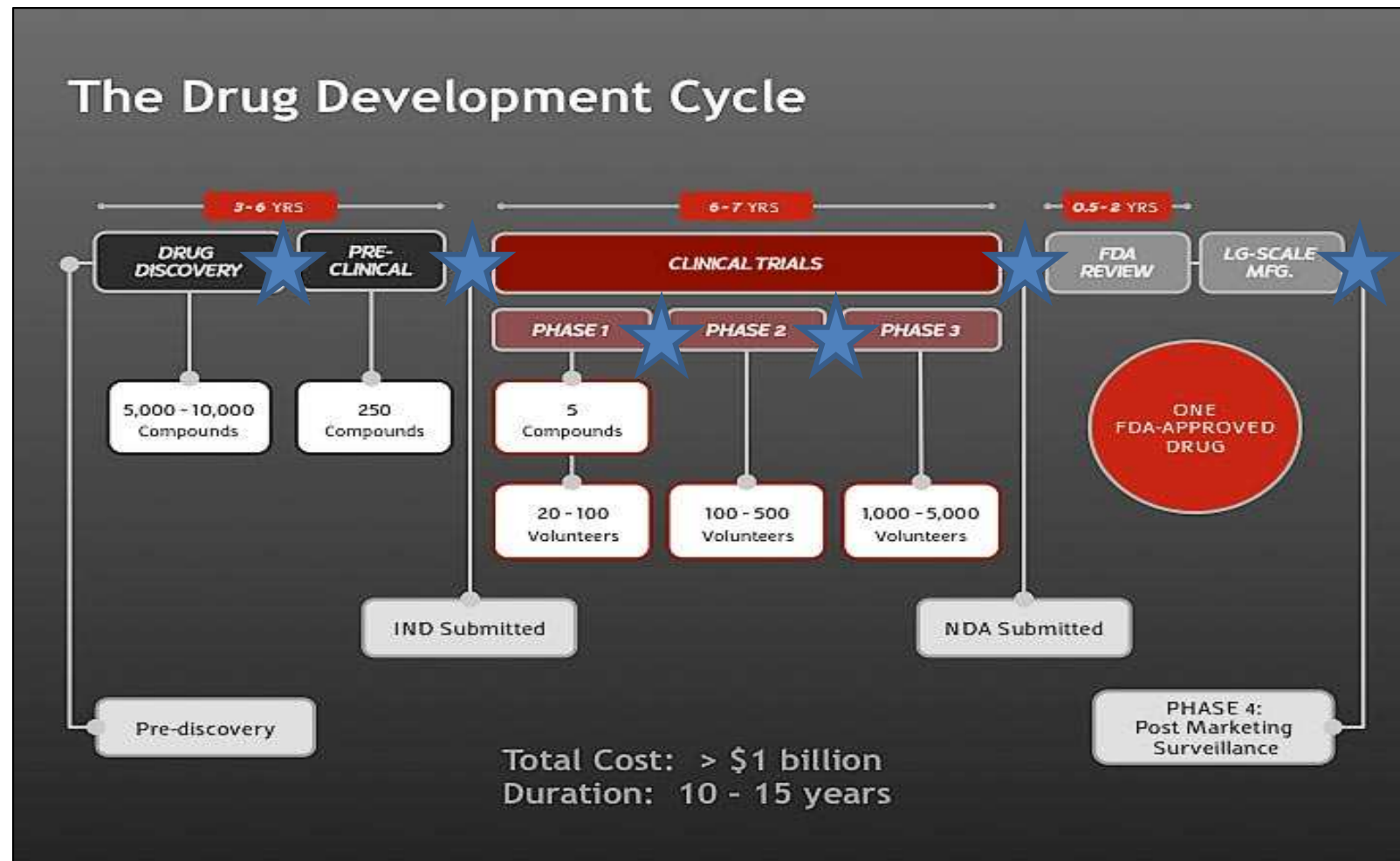
Different pharmaceutical Technology Transfer Project contexts can be managed; each with specific peculiarities; assuming the technology to be transferred is the drug manufacturing process, several possibilities arise:

- *Development to clinical phase TTP*

- *Clinical Phase to Commercialization TTP*

- *Commercial TTP*

Primary Technology Transfer:

- From R&D to production site (industrialization process)
- Intracompany o intercompany

Secondary Technology Transfer:

- From production site to production site
- Intracompany o intercompany
- Pre-submission, post-submission
- Pre-commercialization or during commercialization

Complete and partial Transfers:

- Full manufacturing
- Partial (analytical, release, secondary packaging)
- **Open transfer VS blind transfer**
- **Transfer IN vs Transfer OUT**

© Can Stock Photo - csp25964108

Terminology II

- **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.
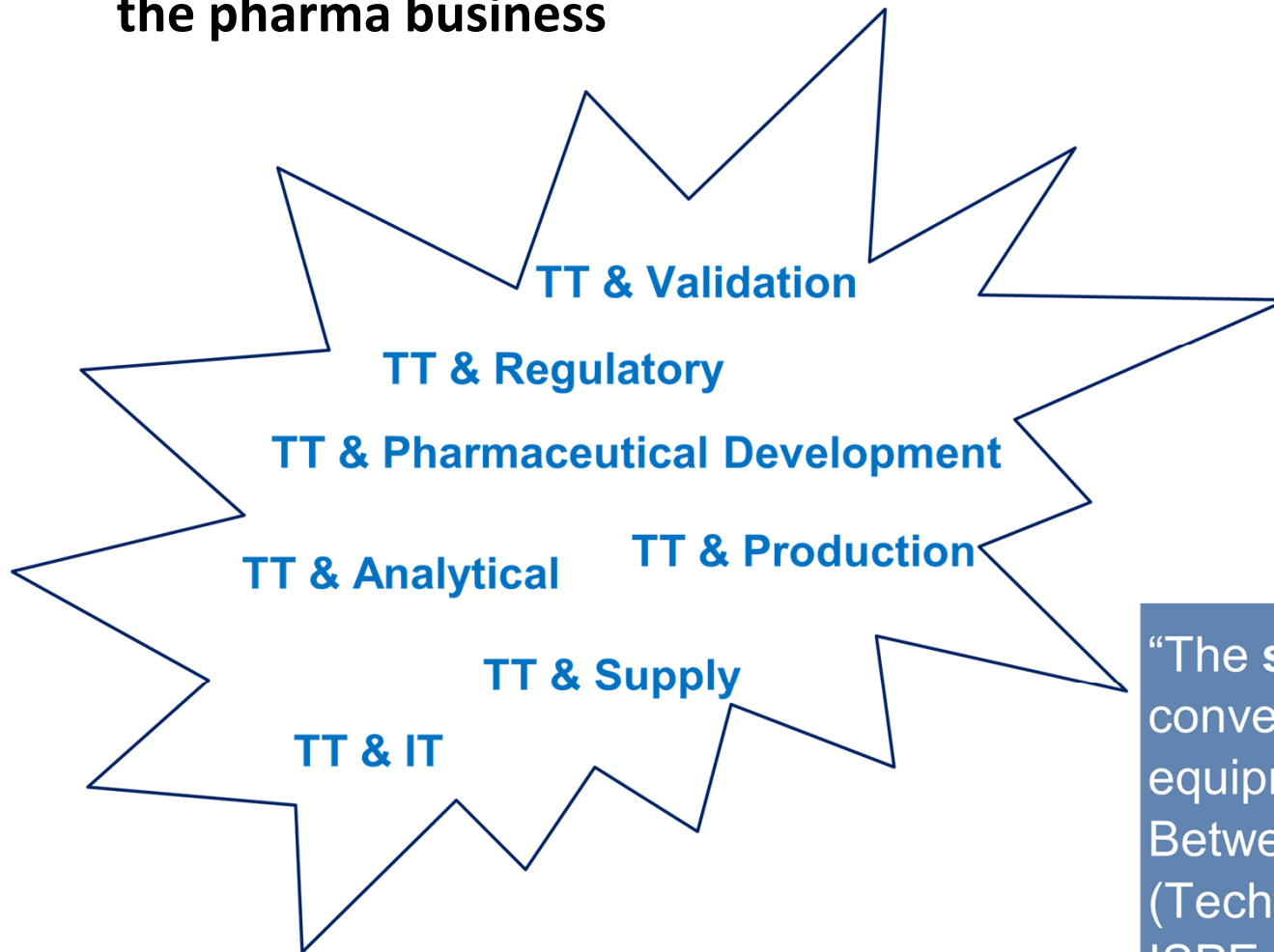
Connecting People, Science and Regulation®
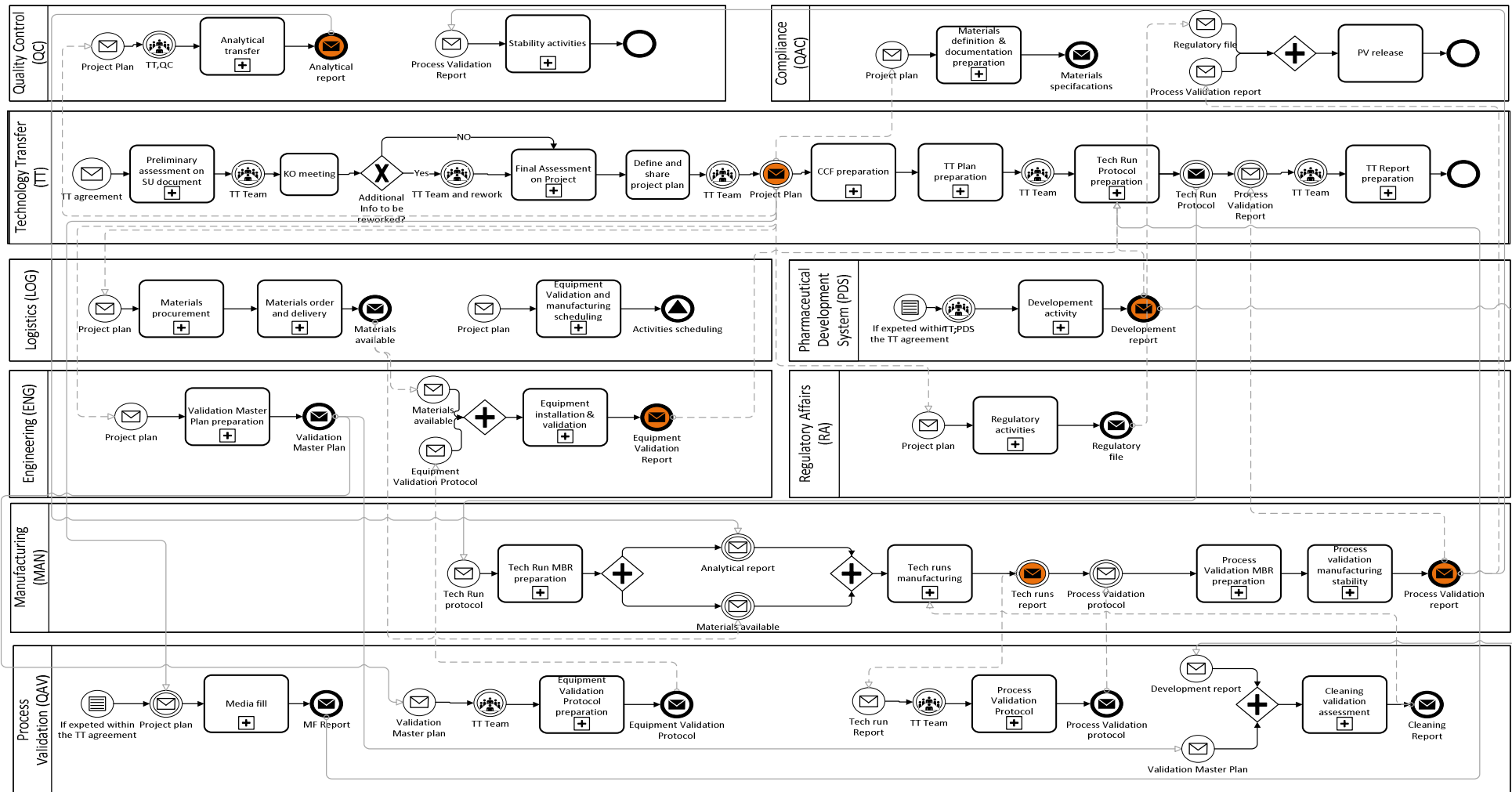
What are the main aspects/characteristics of Technology Transfer?

What makes the Technology Transfer different from the other activities?

- Integration and multidisciplinarity
- Extraordinary activity VS operations
- Complexity
- Unique
- Project Management
- Start-end
- Technical, communication and management aspects
- Hard and soft skills
- ……other…..

PDA ®
Parenteral Drug Association

An integrated process that involves different functions and that is part of the pharma business

TT & Validation

TT & Regulatory

TT & Pharmaceutical Development

TT & Production

TT & Analytical

TT & Supply

TT & IT

"The **systematic** means of conveying ability, documentation, equipment, skills, and systems Between parties"
(Technology Transfer, ISPE, Good Practice Guide, 2003)

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

- 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.
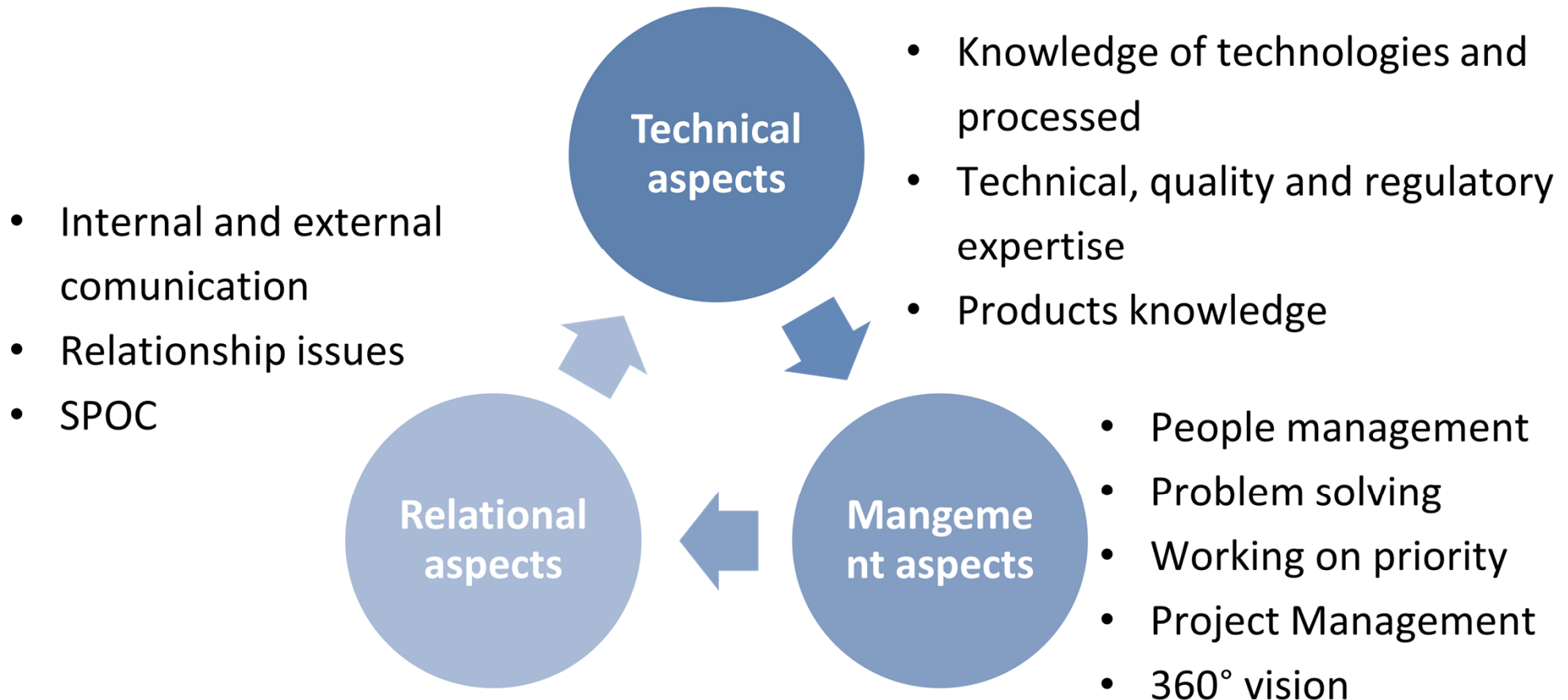
Technical aspects

- Knowledge of technologies and processed
- Technical, quality and regulatory expertise
- Products knowledge

- Internal and external comunication
- Relationship issues
- SPOC

Relational aspects

Mangement aspects

- People management
- Problem solving
- Working on priority
- Project Management
- 360° vision

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).

Success factors:

- Fulfilling **regulatory and qualitative requirements**

- Meeting **projects goals** (timelines, budget, people)

- Fulfilling **technical requirements** (production and analysis)

- **Technology aligments and related evaluation:**
  - Equipments comparison between Sending and Receiving units
  - Scale up evaluation
- **Suppliers:**
  - Evaluation of the suppliers
- Analytical transfer
- Identification of **critical quality attributes**
- Identification of **critical process parameters**
- **Technical batches**

- **Primary technology transfer:**
  - Same type of technology
  - Scale down process
- **Secondary technology transfers:**
  - Which are the equipment in the two units?

Granulator

Lyophilizer
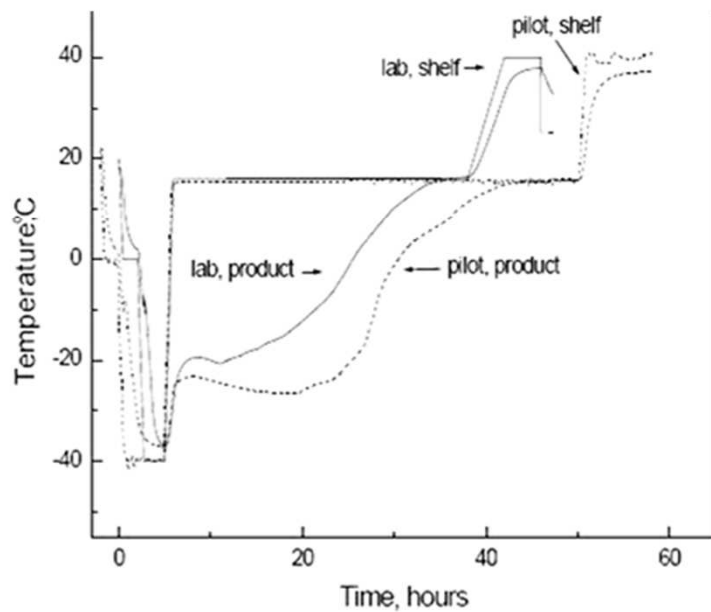
4 Shelfs – 0.5 m^2

Example of industrial scale lyophilization chamber

14 Shelfs - 23 m^2
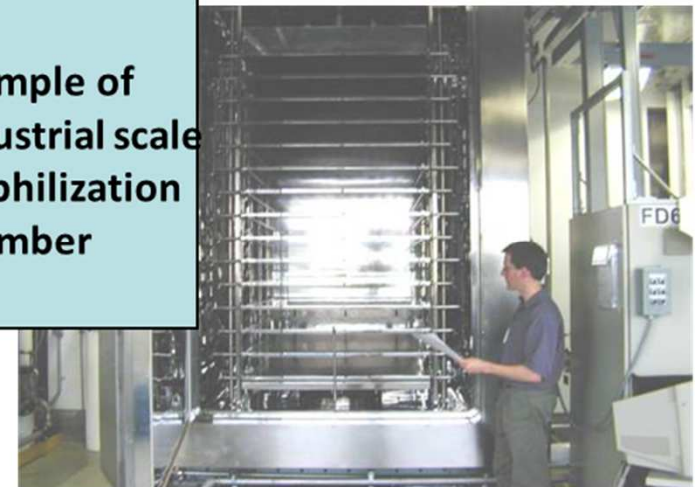
Compression

Loading
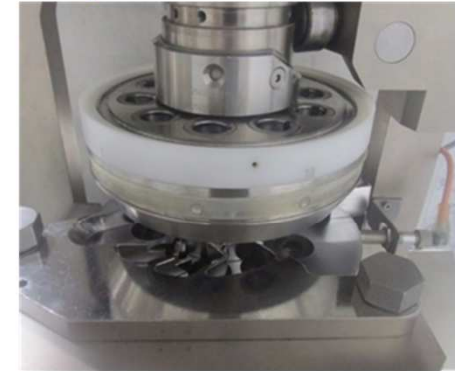
TECHNICAL BATCHES

Definition: batches manufactured at the receiving unit using industrial equipment with the aim to test the process

✓ Strategy is defined depeding from process, risks and budget

✓ Goal is to test the process:

    ✓ The first technical batches are necessary to test the process and highlight the challenges: problems are welcome

    ✓ "Challenge" the process and its limits and to propose solutions

✓ They are a knowledge opportunity for both the units

SUBMISSION BATCHES

Definition: batches manufactured at the receiving unit to support product registration

✓ Strategy is different depending from type of registration, product and market

✓ The can be validation batches also

✓ They are stability batches

✓ They shall be manufactured at industrial scale, with the final process and once analytical transfer is complete

> $\Rightarrow$ **Both technical and submission batches are part of the Technology Transfer!**

Analytical transfer

- It is a crucial phase of the Technology Transfer

- Usually is considered not so impprtant but it is one of the crucial aspects that leads to a successful Technology Transfer

- Different SOPs and practices at Sending and Receiving units can make it complicate

- No connection between Sending and Receiving units can make it more complicate

- Issues in methods validation or not rubust methods can cause issues during the Analytical transfer

- Analytical transfer must be completed before the production of the submission batches
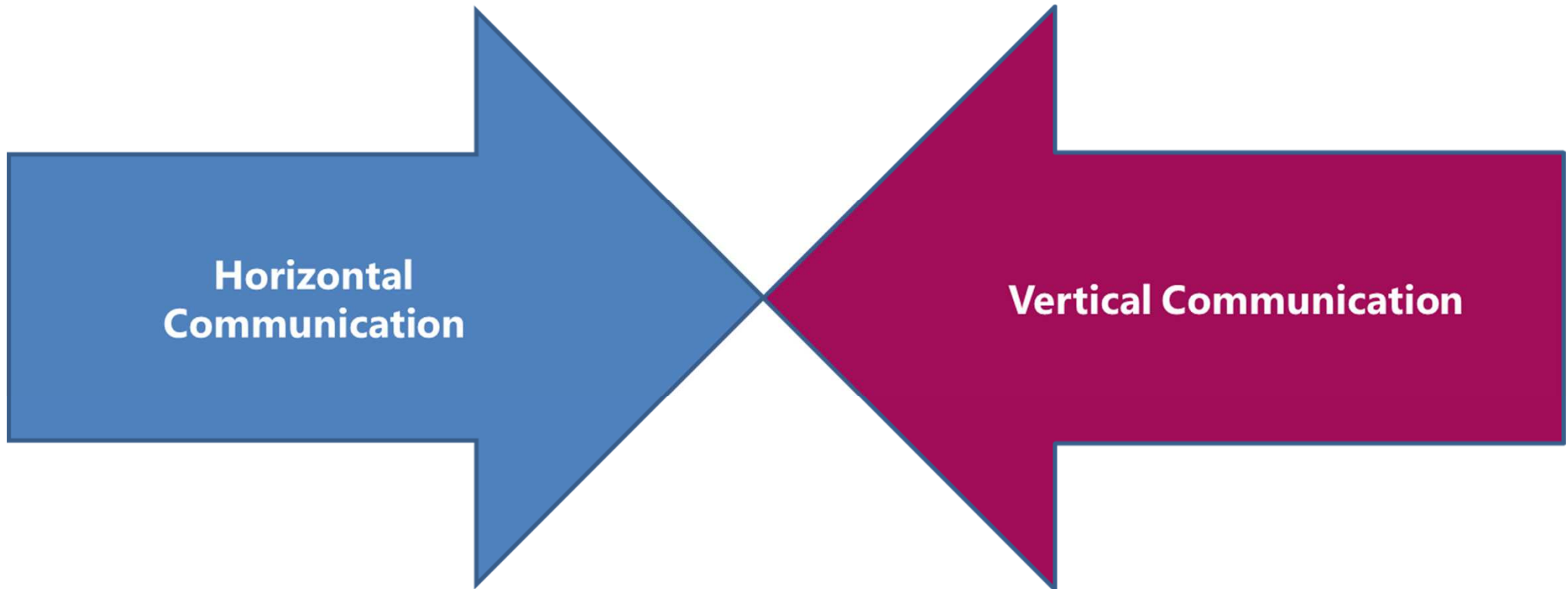
Team construction and management (dedicated slides)

PM role (dedicated slides)

Common goals between the parties:

- Different missions of the parties (i.e. Sending and Receiving units)
- Transfer strategy
- Tech Transfer plan
  - Flexible and agreed
  - Ruled by "change control"
- Status and goals clear and controlled in each phase of the project

Company culture:

- Without a focus of the company there is no success: Technology Transfer is a company project
- Built in long times and with efforts
- Communications barriers shall be destroyed

When to start a Technology Transfer?

- Depening from type of technology transfer: primary, secondary, intercompany o intracompany…..
- **Primary technology Transfer:**
  - Advanced start allows more alignment between development and manufacturing, reduce risk of failures and gives usually better results
  BUT
  - Usually triggers higher investments….and in case of failure?
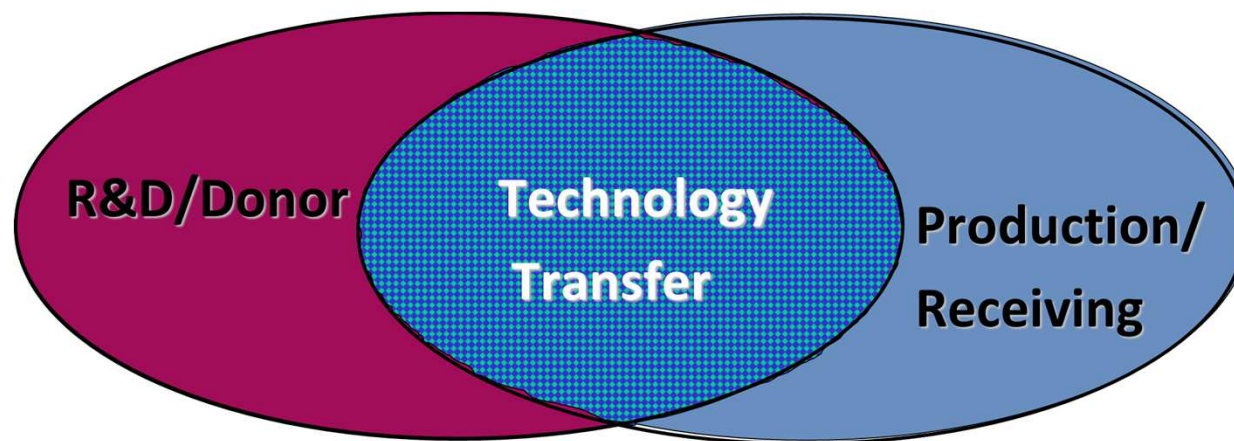
Which are for you the main areas of concern in Technology Transfer: technical, organizational or other?

Connecting People, Science and Regulation®

Technology Transfer in Pharma: main phases

How is a Technology Transfer structured?

pda.org

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

PDA
Parenteral Drug Association

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

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

5 main steps!

4. Licensing & Manufacturing

    a.   Regulatory submission

    b.   Monitoring of the manufacturing batches

5 main steps!

5. Project Closure

    a.   Continuous improvement

    b.   Lesson learned

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).

- Be always focus on Patient as this is our final «Client»

- Multidisciplinary Context

- Dynamic and challenging environment

- Different types of Technology Transfer

- Technical, relational and management aspects

- 2 main risks categories to be considered: project and process risks

Technology transfer GMP aspects

How to manage a Technology Transfer in GMP?

pda.org

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!

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!

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!

Connecting People, Science and Regulation®

- 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 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.

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

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

Team role in Technology Transfer

Is the team critical for TT Project success?

pda.org

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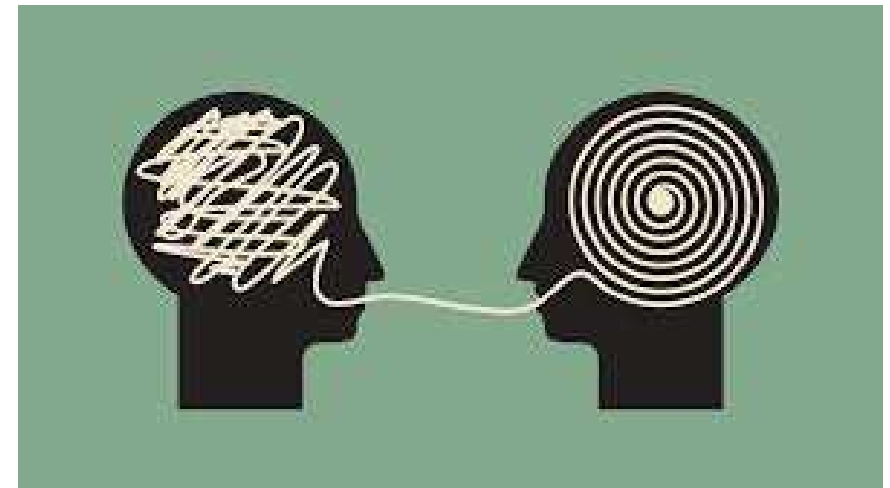
Which are the main Project risks? – PDA TT IG 2018

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*
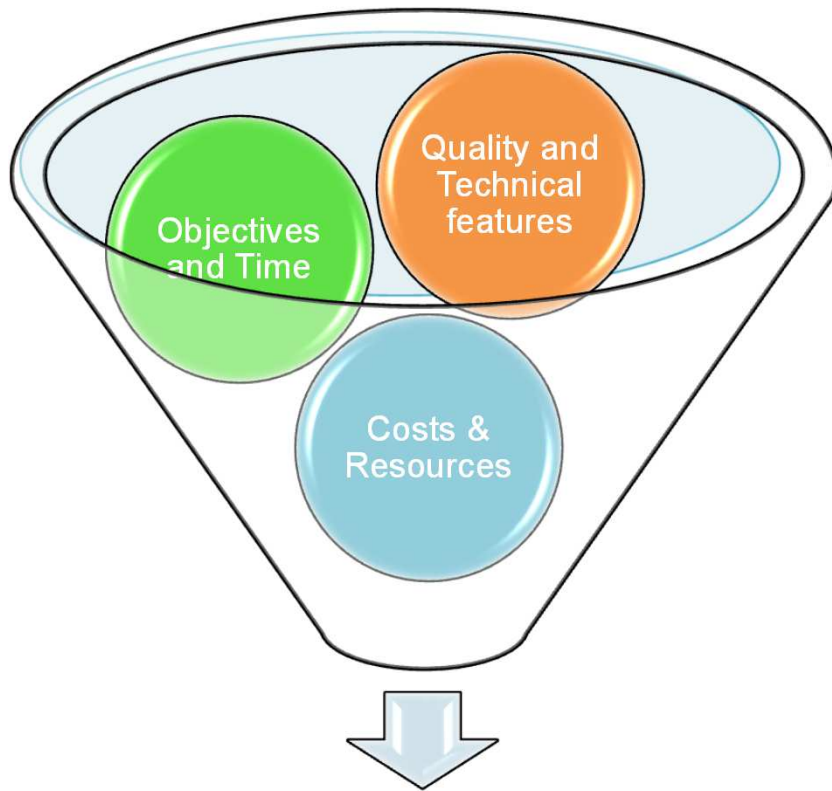
Planning + **Social Intelligence**
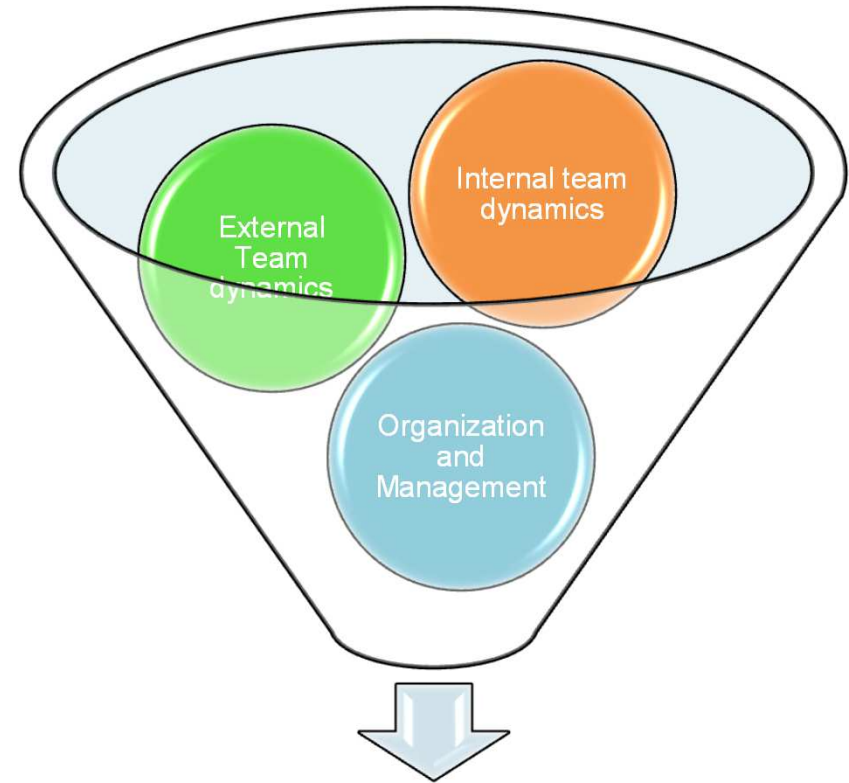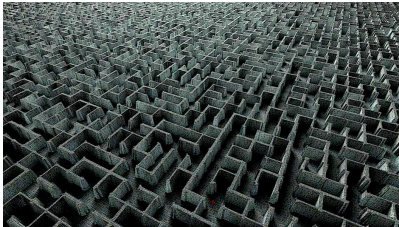
Regulatory
Affairs

Business

Manufacturing

Project
Engineering

Quality

Development

Process
Engineering

Regulatory

Supply Chain

Procurement

Analytical

- 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

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.

Connecting People, Science and Regulation®

- **PM definition:**
  - PM in Receiving site
  - Endorcement del Management=Sponsor
  - Intracompany o intercompany
- **Team definition:**
  - Receiving Unit
  - Sending Unit
  - SPOC=single point of contact in each of them
  - Corporate functions
  - Others

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

```
                          ┌──────────┐
                          │ Director │
                          └─────┬────┘
            ┌───────────────────┼───────────────────┐
            ▼                   ▼                   ▼
     ┌────────────┐      ┌────────────┐      ┌────────────┐
     │  Head of   │      │  Head of   │      │  Head of   │
     │ Function 1 │      │ Function 2 │      │ Function 3 │
     └─────▲──────┘      └─────▲──────┘      └─────▲──────┘
           │                   │                   │
┌──────┐   │                   │                   │
│  PM  │◄──┴─────┐        ┌─────┴─────┐      ┌───────────┐
└──────┘   │ SUL │        │    TTF    │      │ SU Member │
           └─────┘        └───────────┘      └───────────┘
```
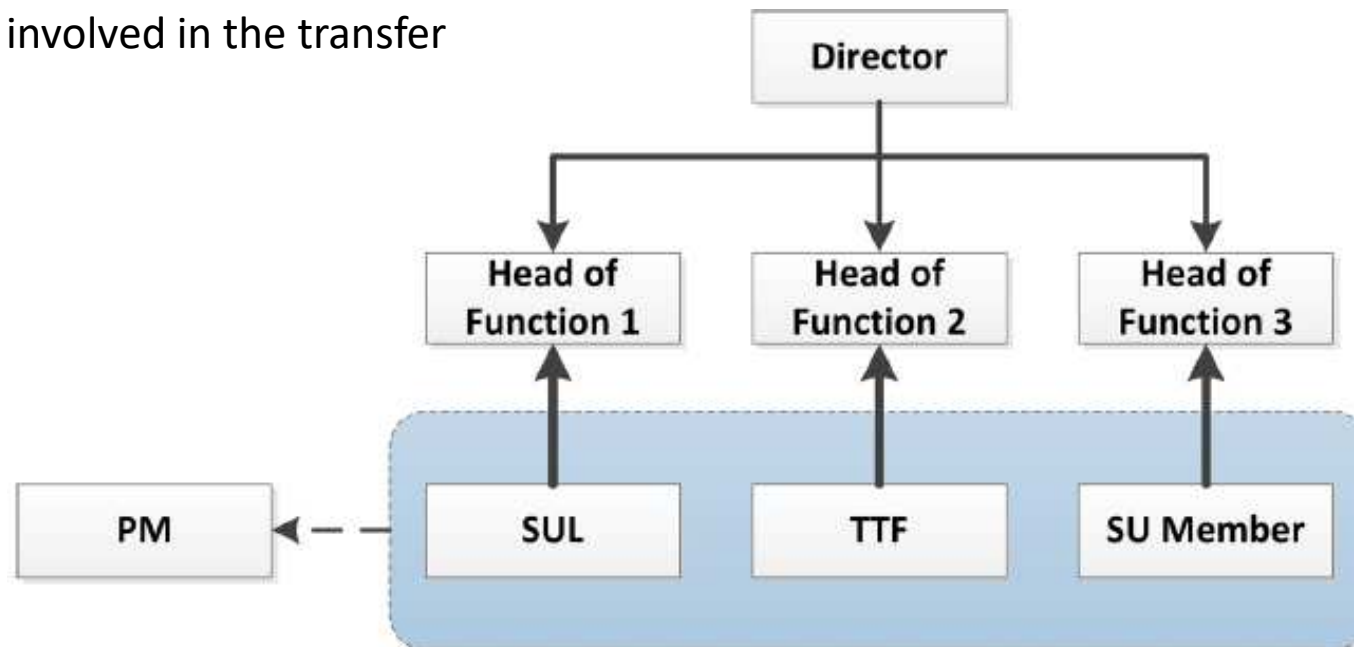
In a hard functional approach, a «Business Unit» is created around the technology transfer needs. Main SMEs report directly to the Technical Lead with a «silos» approach.

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.

Team main phases
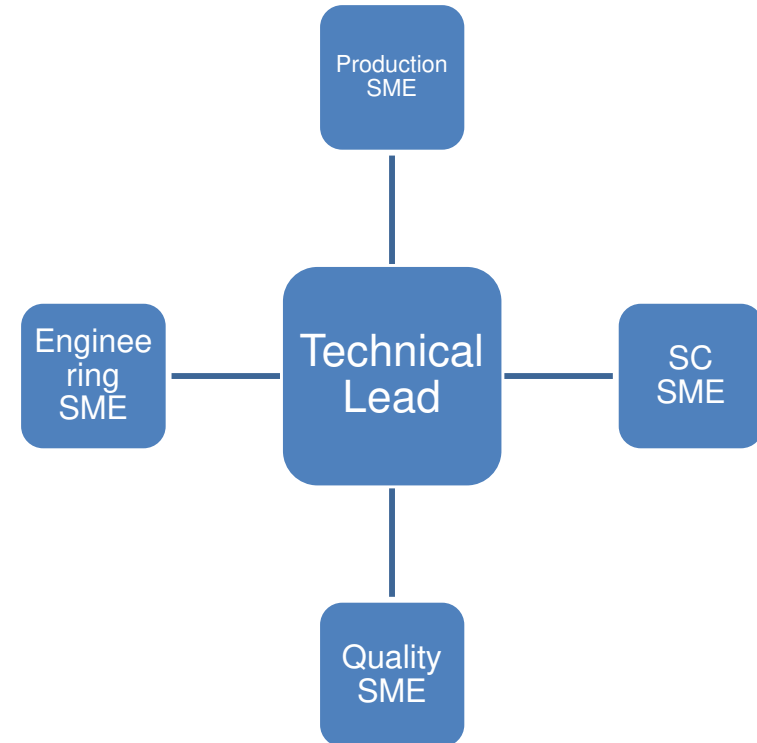
«Group of motivated people that work for a common goal and that cooperate to reach excellents results»

Team lifecycle phases:

Forming	Storming	Norming	Performing

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

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 relationship and management III

#	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
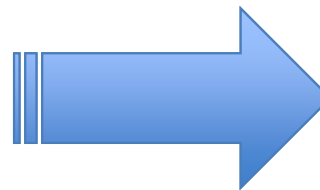
What kind of team do you manage? Which

organizational structure do you use?

Which are the main difficulties in team management?

Stakeholders analysis

Who are the stakeholders and how to manage them?

pda.org

Stakeholders definition I

«**Stakeholder:** people or organization that is actively involved in the project or whose interests may be positively or negatively affected by execution or completion of the project» PMBOK® del PMI®

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

STAKEHOLDER MAPPING
stakeholder mapping
©Study.com

Suppliers

SU Team Members

Unions

Upper Management

Regulatory Agency

RU Team Members

Competitors

Corporate Experts

Employees

Business Partners

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

STAKEHOLDER MAPPING

stakeholder mapping

Study.com

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.

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.

2. Prioritise your stakeholders

Stakeholders register
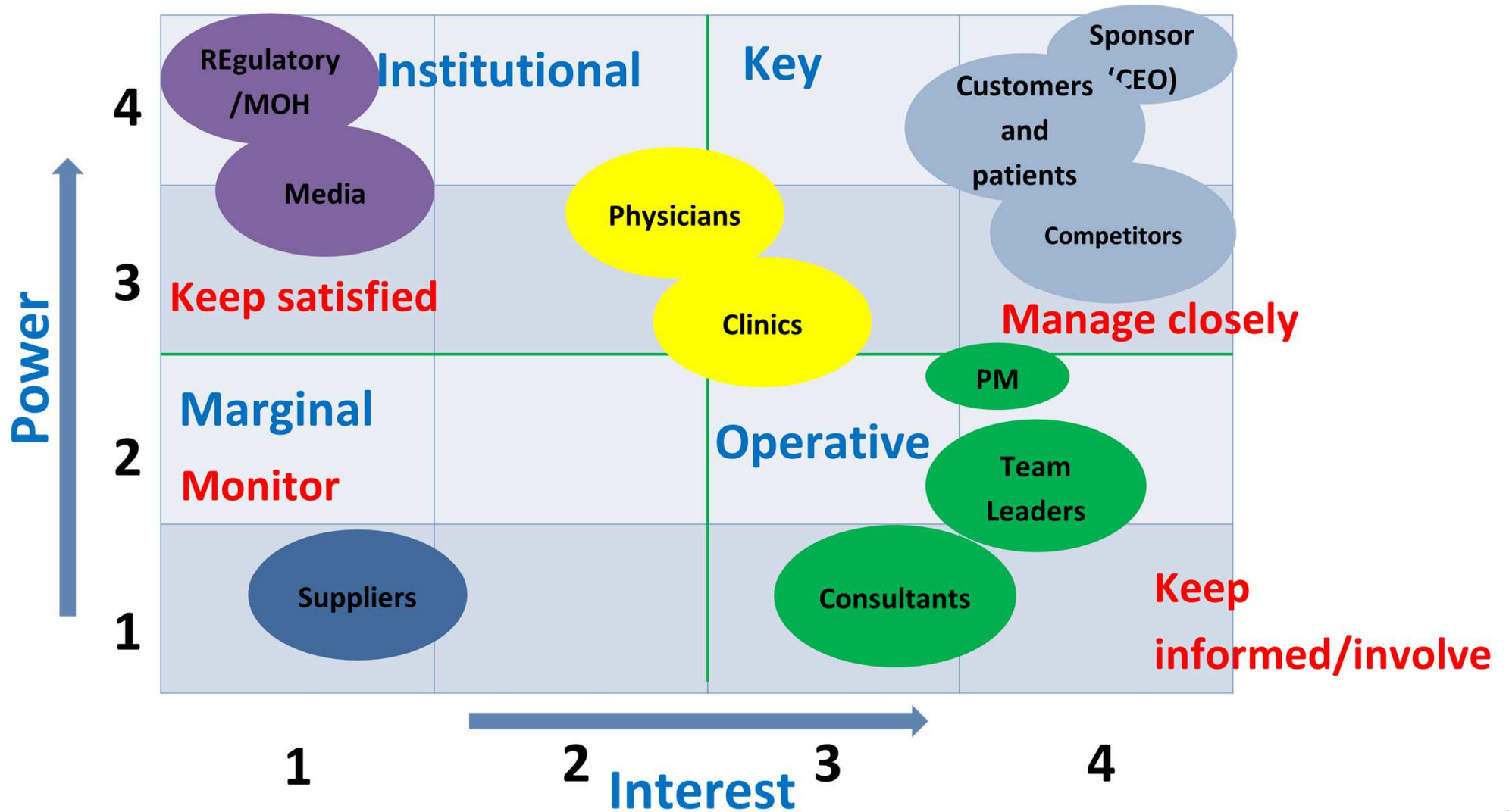
Stakehoder	Stakeholder type	Interest (1-4)	Power (1-4)	Engagement (U, R, N. S. L)
Regulators/MoH	Institutional	1	4	N
Press	Institutional	1	3	N
Suppliers	Marginal	1	1	U
Physicians/Clinics	Institutional/key	2	3	U
Experimental clinica	Institutional/key	3	3	S
Sponsor	Key	4	4	S
Customers/patients	Key	4	4	N
Competitors	Key	4	3	R
PM	Operative	4	2	L
Team Leaders	Operative	4	2	L
Trainers	Operative	4	1	S

U= Unaware, R=Resistant, N= Neutral, S=Supportive, L=Leading

Connecting People, Science and Regulation®

PM Role in pharma Technology Transfer projects

Is the PM critical for TT Project success?

pda.org

- Technical Skills
- Planning
- Multitasking and Organization
- Flexibility
- Troubleshooting
- Negotiation
- Goal oriented
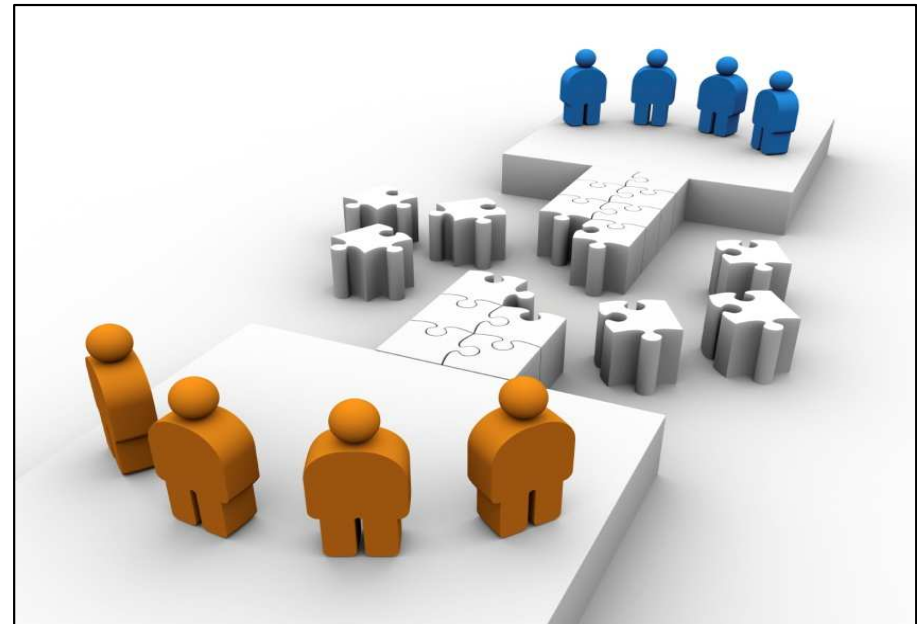
- **TTPMs are the "*General Manager of the project*" for our clients**

- 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**

Connecting People, Science and Regulation®

«**Project charter:** document issued by the Project Initiator or Sponsor that formally authorizes the existence of the project and provides the PM with the authority to apply organizational resources to project activities» PMBOK® del PMI®

Why to issue a Project Charter?

- To endorce the PM
- Nominate the team
- Get the Management approval
- Agree the main pillars with the Sponsors
- Define and officialize Technology Transfer project goals, budget and timelines

NO PROJECT CHARTER NO PARTY

Connecting People, Science and Regulation®

«**RACI =** responsibility matrix where single functions and levels of responsibilities are listed»

R (responsible)

C (consultable)

I (informed)

A (accountable)

PM and responsibilities: RACI II

Project Deliverable (or Activity)	Project Leadership									
Role	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

Connecting People, Science and Regulation®

LEADERSHIP

GUIDANCE SOLUTION VISION TEAMWORK DIRECTION STRATEGY COMMUNICATION GOAL

shutterstock.com • 733723789

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.

102

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.

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 <u>hierarchical authority</u>—*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.

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 <u>hands-off</u> 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 <u>communication and persuasion</u> 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.

- **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!

- Technology Transfer is not possible without a team

- Team shall be managed, organized and motivated

- Role and leadership of the PM are crucial for Technology Transfer success

- Stakeholders are different and shall be managed

PEOPLE ARE CRUCIAL FOR A SUCCESSFULL TECHNOLOGY TRANSFER

Connecting People, Science and Regulation®

What type of Leader you are?

Connecting People, Science and Regulation®

Technology Transfer in Pharma: projects governance and tools

Which does governance mean in TT?

pda.org

Planning

+
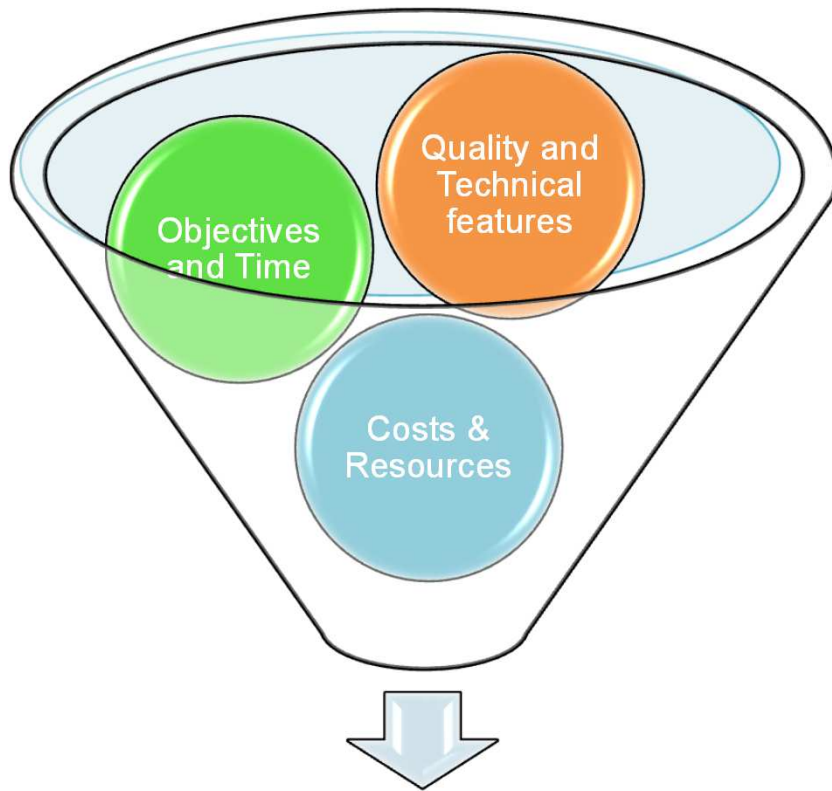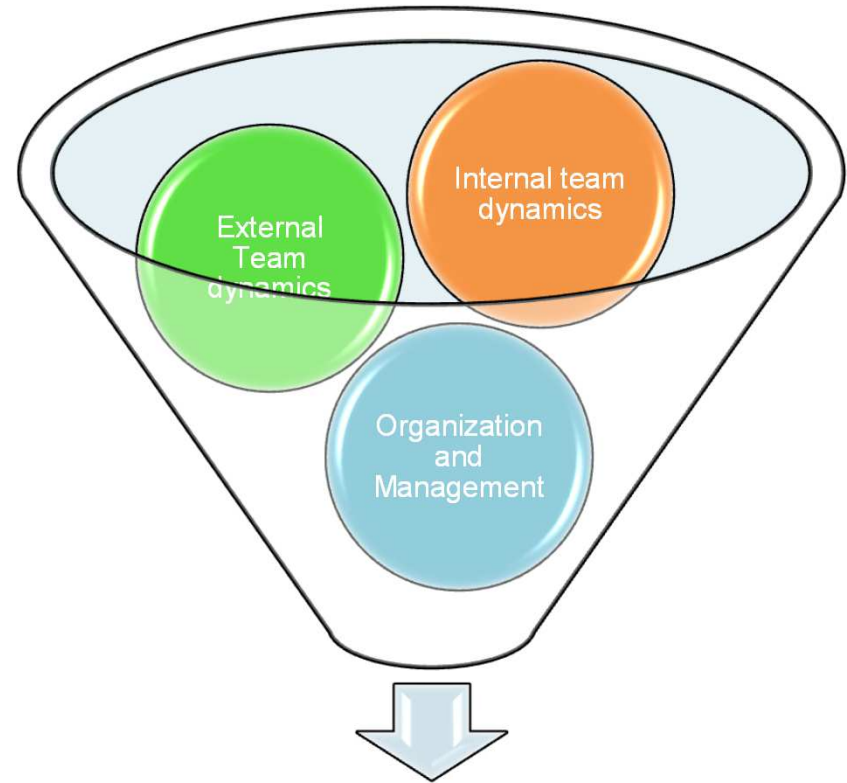
Social Intelligence

Define scope, plan, execute and track

- Project Gantt

- Action List

- Decision List

- Risk Register

- Activities completion tracking

Define what is TO BE be done and

Define what IS NOT to be done

DELIVERABLE: «Any unique or verificable product, result or capability, to perform a service that must be produced to complete a process phase or project»

WORK BREAKDOWN STRUCTURE (WBS):
- Activities are detailed
- Scope is formalized

Work Breakdown Structure:

- Logical structure used to define project deliverables, till the needed level of detail, and to list main project activities needed to reach the goal
- It is necessary to assign responsibilities, define work load and subsequently create the gaant
- It is necessary to formalize the «TT scope» defining not only the deliverables but also the activities needed to reach them

How to create a WBS?

WBS/INNO6-1117

(1) Prototipo realizzato — **(2)** Test conclusi — **(3)** Formazione conclusa — **(4)** Campagna pubblicitaria definita — **(5)** Sottomissione regolatoria effettuata — **(6)** Progetto gestito

(1.1) Primo prototipo realizzato
(1.2) Prototipo definitivo realizzato
(2.1) Test definiti
(2.2) Test svolti su prototipo
(2.3) Prototipo validato
(3.1) Organizzazione formazione conclusa
(3.2) Formazione completata
(4.1) Contratti con riviste del settore firmati
(4.2) Design pagine pubblicitarie realizzato
(5.1) Dossier tecnico emesso
(5.2) Dossier tecnico sotttomesso

(1.2.1) Fornitura dei componenti per la realizzazione dei prototipi
(1.2.2) Assemblaggio del numero di prototipi definitivi necessari.

(2.2.1) Svolgere test (ufficio R&D)
(2.2.2) Esecuzione protocollo clinico

(2.3.1) Definire parametri validazione
(2.3.2) Validare prototipo

(3.2.1) Eseguire formazione
(3.2.2) Completare test di apprendimento

(4.2.1) Definire design pagine pubblicitarie
(4.2.2) Approvare pagine pubblicitarie

(5.2.1) Pagamento fee sottomissione
(5.2.2) Sottomissione dossier a MoH

(1.1.1) Definire requisti tecnici
(1.1.2) Definire materiali di utilizzo
(1.1.3) Definire design
(1.1.4) Definire elettronica di controllo
(1.1.5) Eseguire l'assemblaggio

(2.1.1) Definire parametri valutazione per design ed utilizzo
(2.1.2) Definire i test da svolgere (ufficio R&D)

(3.2.1) Prenotare sala formazione
(3.2.2) Definire date giornata di formazione
(3.2.3) Definire materiale necessario per formazione
(3.2.4) Definire lista partecipanti

(4.1.1) Definire riviste da contattare
(4.1.2) Organizzare meeting con riviste scelte
(4.1.3) Chiudere contratti con le riviste scelte

(5.1.1) Raccogliere documentazione tecnica
(5.1.2) Redigere dossier tecnico

WP (Work Packages)

114

ASSIGN RESPONSIBILITIES
- For each of the activity assigned clear resposnibility (RACI or other models)

ESTIMATE THE EFFORTS:
- Expert judgment:
- Parametric estimation
- Analogous estimation
- Lesson learned
- Bottom up estimation
- Top down estimation

ASSIGN THE RESOURCES

CONVERT THE EFFORTS IN DURATION

ESTABLISH THE RELATIONSHIP BETWEEN THE ACTIVITIES

DEFINE THE PROJECT PLAN

Activities relationships
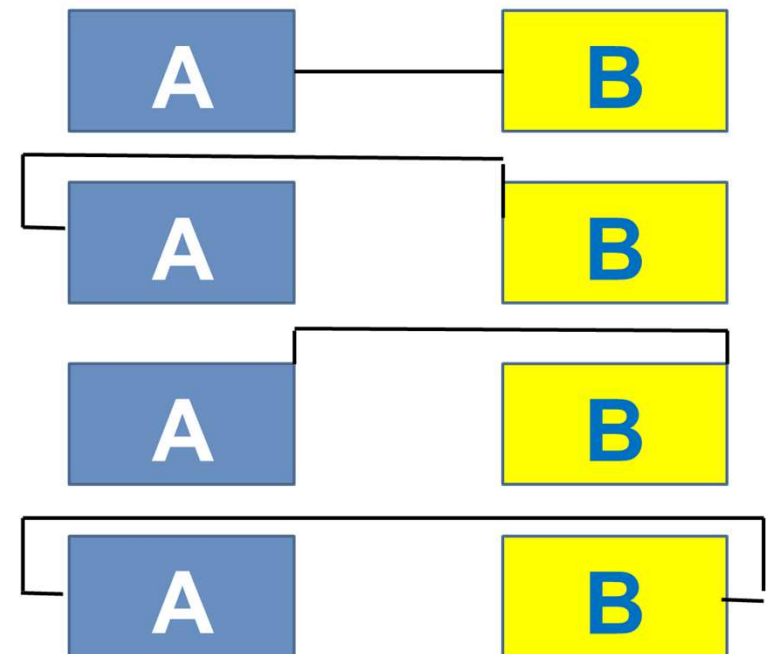
ACTIVITY LIST	PM	HR	ING	MAN	QA	PROCUR	FIN	MARKETING	IT	QA/VAL	R&D	PROD	COMM	RA	CLINIC
(1.1.1)			120	80	120					80	80		40		
(1.1.2)			120	80	40					80	80		40		
(1.1.3)			80								120		40		
(1.1.4)			40		160										
(1.1.5)			20	20	20							200			
(1.2.1)						80	80								
(1.2.2)			20	20	20					40	40	200			
(2.1.1)			60						20	40	160		40		
(2.1.2)			120							40	80			40	40
(2.2.1)			40	20	20				10	80	200				
(2.2.2)			160							40	80				220
(2.3.1)			8							16	8	8		16	
(2.3.2)			50	50	50	50			20	160	40	40	40		
(3.1.1)		20												20	
(3.1.2)		40												20	
(3.1.3)		40				40	40							40	
(3.1.4)		40												80	
(3.2.1)		160	40	40	40				20	20	40	40		80	
(3.2.2)		160	20	20	20					20	20	20		40	
(4.1.1)								40		20	20			20	
(4.1.2)								80						20	
(4.1.3)						40		80							
PM	720														
N° hour/am	720	460	1258	390	550	210	120	520	70	776	1028	508	560	536	300
Cost/hour	€ 30,00	€ 20,00	€ 30,00	€ 30,00	€ 30,00	€ 16,00	€ 16,00	€ 30,00	€ 16,00	€ 40,00	€ 26,00	€ 26,00	€ 50,00	€ 30,00	€ 60,00
Total cost/area	€ 21.600	€ 9.200	€ 37.740	€ 11.700	€ 16.500	€ 3.360	€ 1.920	€ 15.600	€ 1.120	€ 31.040	€ 26.728	€ 13.208	€ 28.000	€ 16.080	€ 18.000

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%

Plan and track diagrams VI

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%

TECHNICAL DATA PACKAGE:

- Package that includes all the main information about the product, process, specifications etc from the Sending Unit
- Different dipending from the type of project

TECHNOLOGY TRANSFER PLAN OR PROTOCOL:

- Document that list scope, timelines, activities, responsibilities…..all about the project
- Management document or technical document?
- Different depending from the type of the project
- Different in different organizations

TECHNOLOGY TRANSFER REPORT:

- Document that sum up project conclusions and results
- Management document or technical document?
- Different depending from the type of the project
- Different in different organizations

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

And once the transfer is completed?

Connecting People, Science and Regulation®

Post Technology Transfer

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.

MONITORING PRODUCT, PROCESS, RESULTS
CLOSING PHASE
LESSON LEARNED

….LEARNING IS A CONTINUOUS PROCESS…..

Technology Transfer in Pharma: projects risk management

What does RM mean in TT?

pda.org

- **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

PDA
Parenteral Drug Association

Stability Q1A - Q1F

Analytical Validation Q2

Impurities Q3A - Q3D

Pharmacopoeias Q4 - Q4B

Quality of Biotechnological Products Q5A - Q5E

Specifications Q6A- Q6B

Good Manufacturing Practice Q7

Pharmaceutical Development Q

Quality Risk Management Q9

Pharmaceutical Quality System Q10

Development and Manufacture of Drug Substances Q11

Cross-cutting Topics

132

- 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.

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.

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

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."
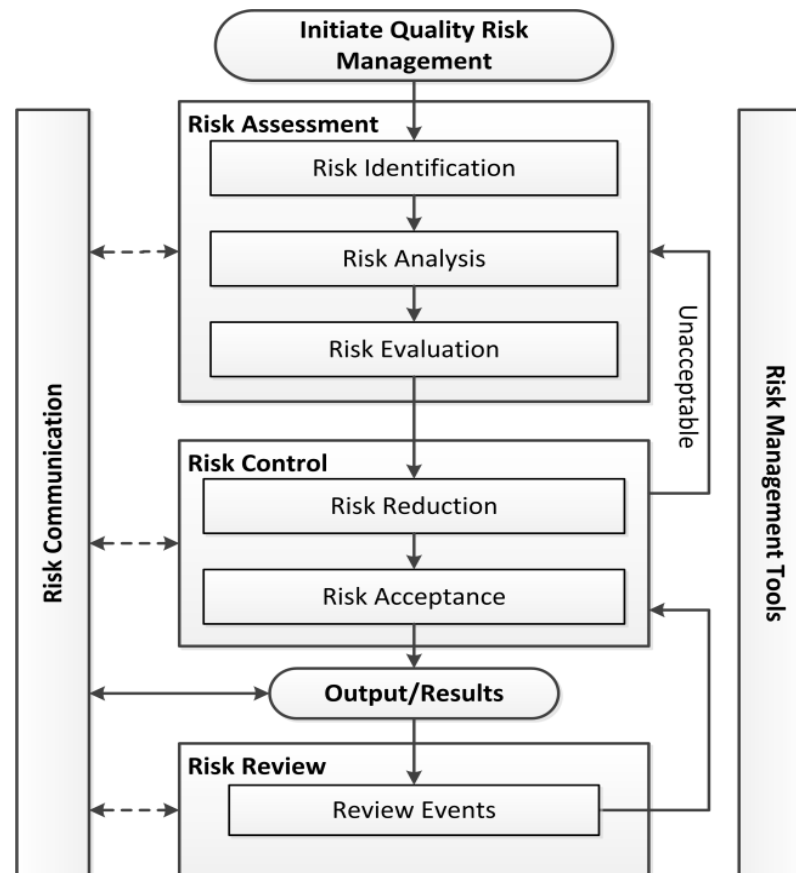
Risks of Technology Transfer

❑ 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

❑ 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

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

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)

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

141

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.
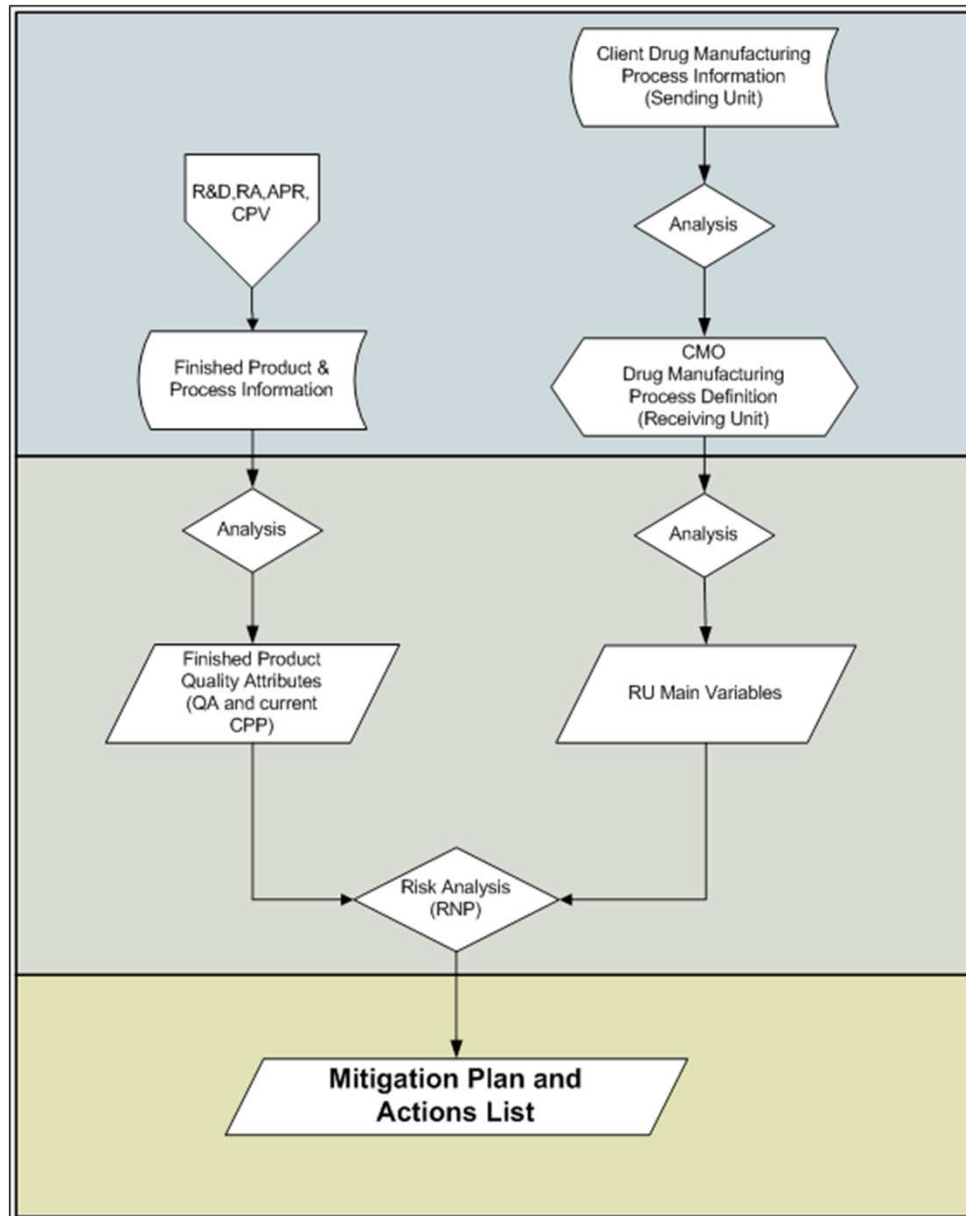
It can be rate based on the table below

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

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

143

Data collection

Data evaluation

Data use

144

Our Risk Assessment and Mitigation approach is based on several Source of information, linked to create a TT Starting Story
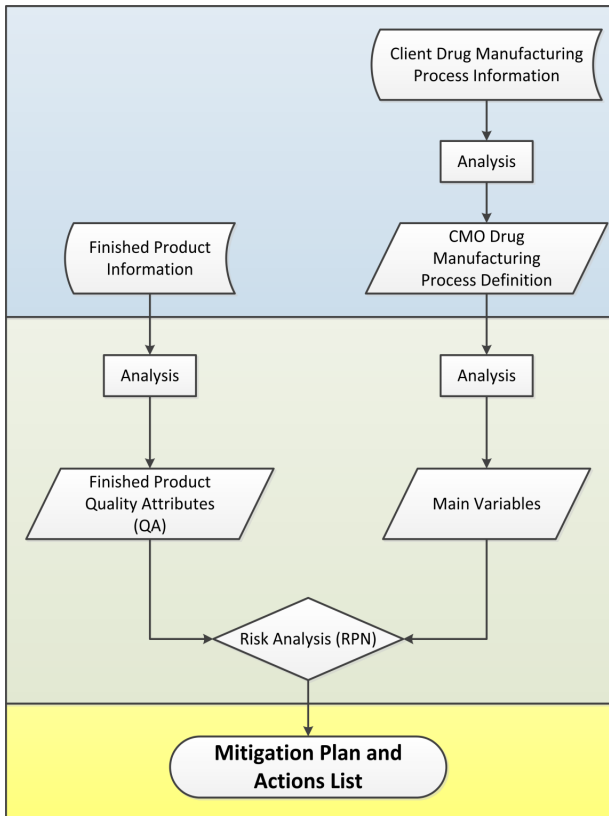
Source 1 – Definition of the Main Process Variables of the product (SU -> RU) *(examples below)*

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

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

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.
		Osmolality	Dissolution speed is insufficient for complete dissolution and a homogenous system.	3	3	1	9	Mixing studies will be agreed on by the SU and performed during the engineering batch.
		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.

. .7

Identify the risks using affinity diagram

Capture   Group   Label

Connecting People, Science and Regulation®
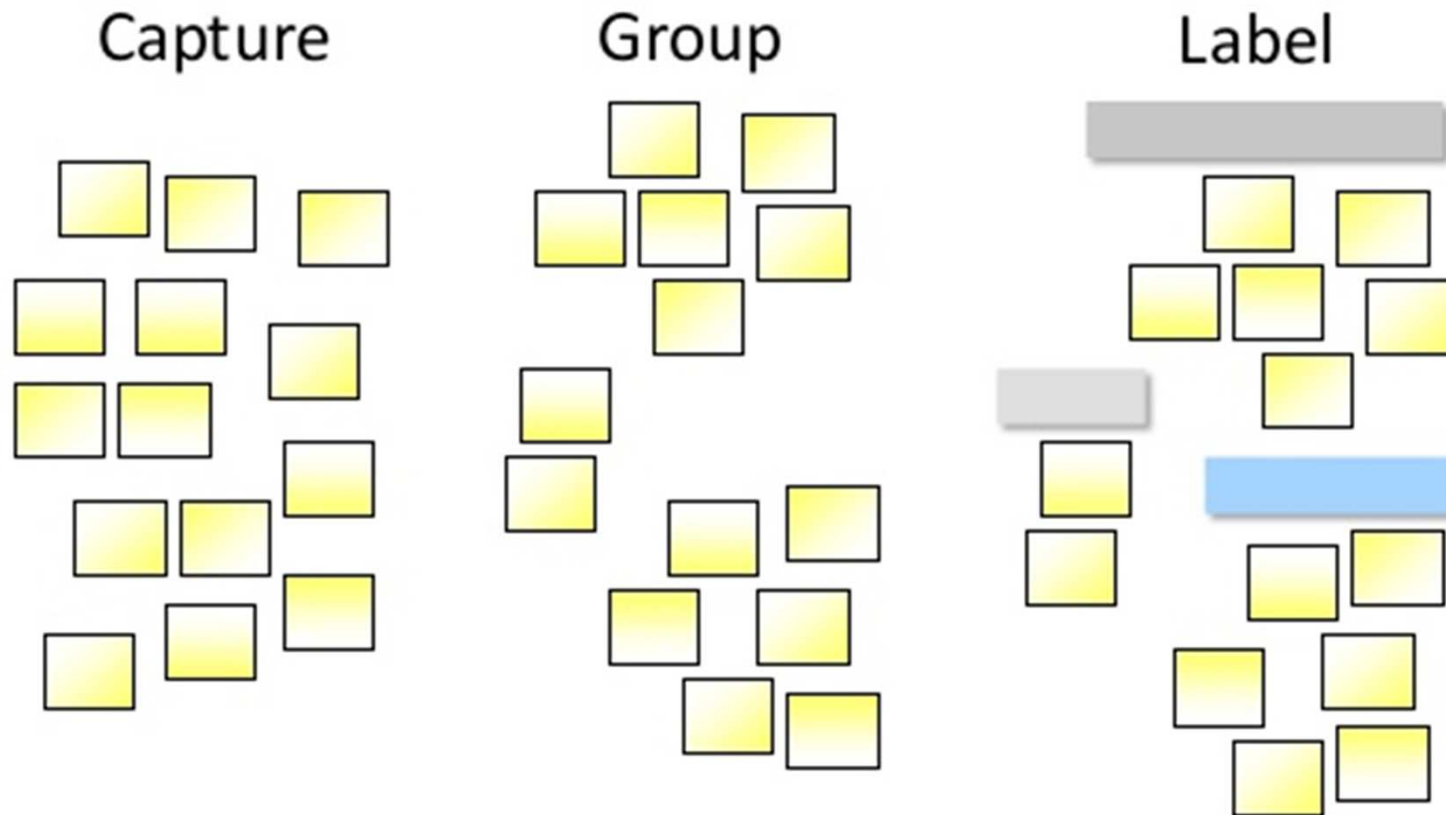
Change Management in Technology Transfer

How to manage changes?

pda.org

Change Management in TT II

- Changes are frequent in TT project execution and can have big impact on project success

- Change management is not an easy skill to establish, train and improve

- Change management is time/costs/resources consuming

- Human nature tends to avoid or delay changes

- Team members are not challenged or selected for change management skills but based on technical skills usually

Change Management is a quite big issue in TT Project and special focus has to be done on team ability to handle change

Managing Complex Change

Vision	+ Skills	+ Incentives	+ Resources	+ Action Plan	=	**Change**
■	+ Skills	+ Incentives	+ Resources	+ Action Plan	=	**Confusion**
Vision	+ ■	+ Incentives	+ Resources	+ Action Plan	=	**Anxiety**
Vision	+ Skills	+ ■	+ Resources	+ Action Plan	=	**Resistance**
Vision	+ Skills	+ Incentives	+ ■	+ Action Plan	=	**Frustration**
Vision	+ Skills	+ Incentives	+ Resources	+ ■	=	**False Starts**
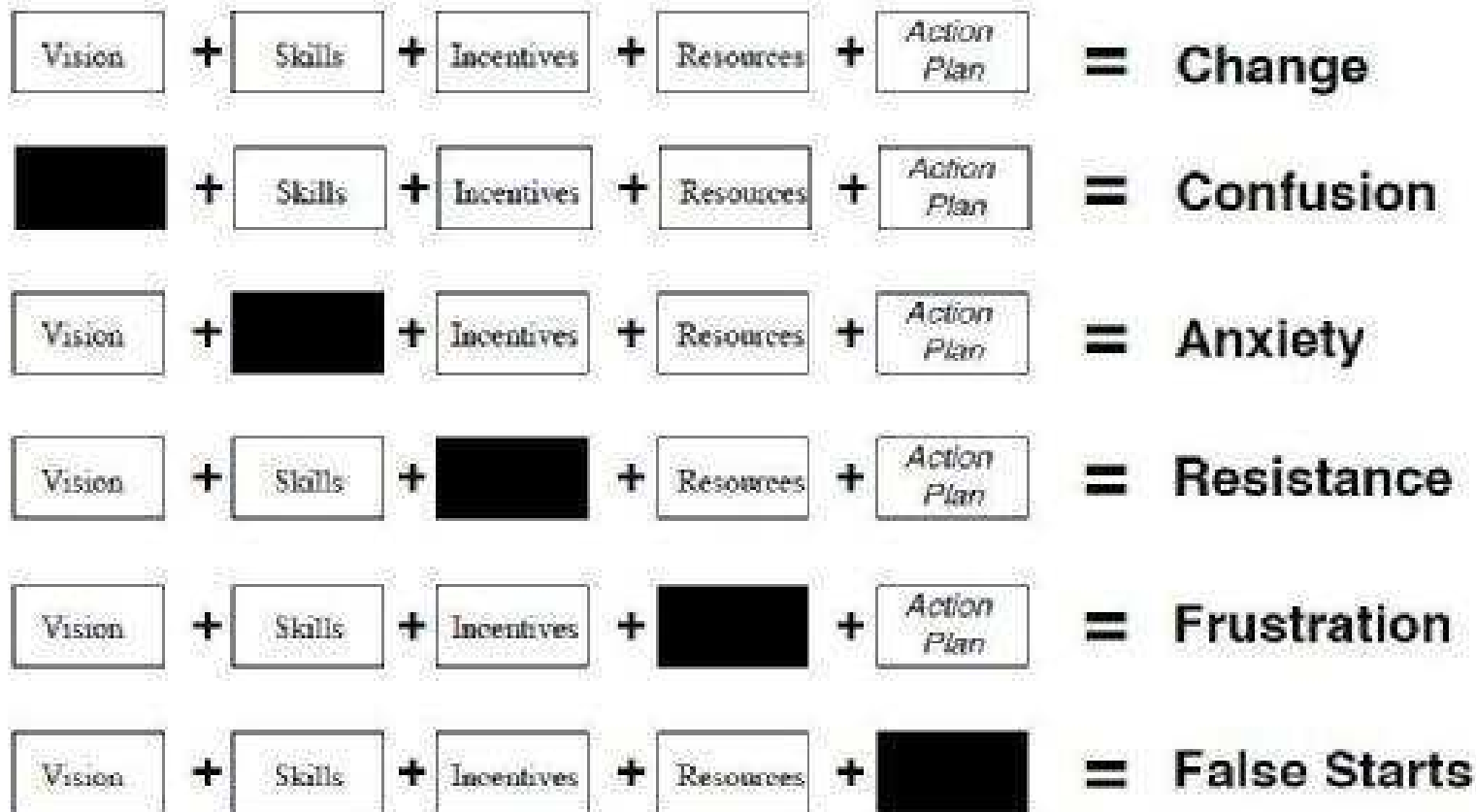
Adapted from Knoster, T., Villa R., & Thousand, J. (2000). A framework for thinking about systems change. In R. villa & J. Thousand (Eds.), Restructuring for caring and effective education. Piecing the puzzle together (pp. 93-128). Baltimore: Paul H. Brookes Publishing Co.

Top three reasons which stops change management

- 1.Day-to-day tasks are overwhelming to most

- 2.There isn't a lot of alignment around what exactly organizational priorities

- 3.Even if the executives understand the priorities, that doesn't mean there's alignment between that and the daily work

This is, in essence, why change management is hard. Moreover….

Several terms connected with change management are "fluffy" (mindset, vision, strategy)

Tips:

- Standard Procedures in place to handle changes from a Business (Costs/Timelines) perspective

- Standard Procedures in place to handle GMP changes

- Escalation process in place and standardized

- Communication process in place and standardized

Change management does need to start with senior decision-makers, which is incredibly fraught: these guys are evaluated differently, their overall picture of issues and strategy is different from yours; overall they perceive the organization and its strengths/weaknesses at a much different level than the people who actually need to be boots on the ground in the change management process.

154

Always starts with three things:

- **Care:** Why are we doing this change management process? Why are we doing it now? Is it because we might get disrupted? Are we fundamentally not able to compete anymore? Are we financially behind? What's the purpose of the change management now?

- **Listen:** Listen all over the org. and listen to your team! These people are closer to the "floor" and know stuff. They get the pain points. They know what we need to change and how. Too often, we believe hierarchy = formal power (yes, still true) = those people know what's best. That's where the logic falls off a cliff. Listen to the upper management to to understand long term strategy and mix the two levels…understand in the specific project moment you are which is the most important for the project success.

- **Align:** Everyone misses this area, and it requires a lot of work…When I say "align," here's the deal.

Technology Transfer and Risk management in real life

Case studies

Case studies: examples of mistakes

- Use of excipeint different from the one used by Sending unit (different content in water) in Injectable product alcohol based: results at the limit of specifications

MISTAKE IN COMMUNICATION

- Delay in the project related to lack of communication on lab instrument needed and so bought with delay

LACK OF COMMUNICATION

- Low yieald and high % of breackage on Mannitol based Lyo product due to reduced N° trials and demo batches

TECHNICAL MISTAKE

- Delay in the project due to change in regulatory strategy

WRONG STRATEGY

Info coming from development department: API oxidizes quickly if exposed to Air/O2. Dispensing is done under N2. Small quantity per batch: approx. 0.8 g per 95Lt of bulk solution

- Main commercial variable considered: Dispensing
- QA Impacted: Impurity Profile & Assay
- Severity 3 – Occurance 3 – Detection is 1
- Risk acceptance level was < 6

Mitigation Plan: Purchase and installation of a Dispensing Hood allowing O2 residual less than 0,5% during dispensing

- QA Impacted: Impurity Profile & Assay
- Severity 3 – Occurance 1 – Detection is 1
- Risk acceptance level was < 3

First TT Batch failed for API assay
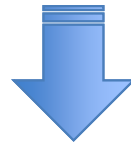
Investigation identified the root cause in the Dispensing Hood

The N2 atmoshpere created with the hood enhances the «electrostatic charge environment» which impacts the accurancy of the API weight

Action: development activities to explore «API oxides quickly»

Mitigation Plan: Defined an appropriate holding time of dispensing based on degradation/stability of the API in Air

Connecting People, Science and Regulation®

- Commercial site (big pharma) located in EU

- The site is a center of excellence for Analytical technology within the network

- The site has an intense Innovation program on analytical technology and a periodic gap analysis is done on analytical equipment to identify "aged" instrumentation

- The current AA-ABS / IPC equipment was identified as critical –> replacement program was put in place

Major Risks/Actions identified:

- Gap Analysis on all the methods done on the equipment and mitigation plan for implementation (including disposable equipment/reagents/utilities/Spare parts)

- Gap Analysis on the knowledge and training program within the lab

- RA Gap Analysis to identify RA actions

- Benchmarking on the network to get information available technique already in place somewhere else

- Technology replacement was succesfully completed on time and on budget
- No issue in knowldege and use of the equipment
- One of the well established process in the plant starts to give issue in IPC
- IPC requires AA-ABS and was impacted by the replacement of the instrument
- The quantitation limit of the new equipment was 100x more that the old one
- Small variation of concentration (Δppm) was detected and re-calculated based on the dilution steps done in lab, brings assay out of IPC range

IPC assay range during process dilution was establishes based on the old analytical technique. No assessment was done during analytical method implementation on manufacturing process, impact on operations missed

- Commercial site (CDMO) located in EU
- They receive a new process (lyo sterile small molecules) from a client in EU
- Process Technology is well known
- Process is already commercial with a good pack of technical information and well knwon commercial story (APR, dev, complaints, etc)
- Scale up or down are not part of the TT, same BS is transferred
- Analytical package is well transferred as well and not new methods are implemented in the R lab
- Process flow is mantained equal to previous one including equipment and primary packaging
- Secondary packaging is not part of the transfer
- Lyo cycle was developped and well established

Major Risks/Actions identified:

- RA completed as one single team, between RU & SU; major risk was the difference in lyo equipment

- Development activities planned focusing on operative parameters during the cycle (T ranges and P ranges during lyo steps) and potential impact on product quality (KF, appearance, reconstitution, impurity profile, lyo texture)

- No concerns based on lyo small scale tests -> Pre-PPQ planned done

Results

- Pre-PPQ 28% of collapsed vials
- RC analysis -> Different T of the product during freezing and primary drying step
- Process Analysis -> ΔT causes in the process ?

lyo chamber T at the beg of the lyo cycle after cip/sip cycle, due to different cooling down procedure. Evaluation done in small scale (not rapresentative of real commercial conditions); robustness not repeated.

- Medium-small company family owned – new product to be transfered to CDMO for capacity issue
- Basic Process Technology and well established
- Process characterization well done and scale-up studied already completed
- Analytical package is well transferred as well and not new methods are implemented in the R lab
- Process flow is mantained equal to previous one including equipment technology and primary packaging

Major Risks/Actions identified:

- RA completed as one single team, between RU & SU; major risk was the difference in scale-up from SU and RU but studied already done to evaluate impact in QA

- Equipment gap analysis completed with no major risks

- Standard challenge pack considered in the first Eng batch due to scale-up

- Pre-PPQ planned and succesfully completed

- PPQ completed succesfully

PDA
Parenteral Drug Association

Results

- TT went very well, according to plan and budget

SO WHAT?

- Commercial production start delayed of 2 years

- API supplier had 483 due to compliance issue, not backup supplier validated to speed up the overall TT (DS+DP)

- New API supplier needed and commercial supply disrupted

Product A:

- Sterile solution in vial and high potent
- Complex formulation

Partial Technology Transfer:

- Production splitted in: bulk production and fill&finish
- Transfer of fill&finish, analysis and release

Partially blind transfer:

- No contact with the current manufacturer but only with the MAH

Main Challenges:

- Complexity of the production process (new for the receiving site)
- Manufacturing process defined by MAH and current manufacturer with no involvment of the receiving unit
- No contact with the current manufacturer/information only from MAH
- Strict timelines

Collect information

- Collect as much info as possible from MAH
- Involve MAH in all the discussions with suppliers and technical decisions
- Get knowledge on the new manufactuing process

Definition of manufacturing equipment:

- Carefully evaluate data received from MAH
- Comparison of the two sites equipment
- Evaluate the two options in case of difference:
- Use available equipment
- Introduce new ones

Receiving site equipment

Class C compounding room

Class A/B filtration & filling room

Controlled area (external vials washing oom/load-unload autoclave)
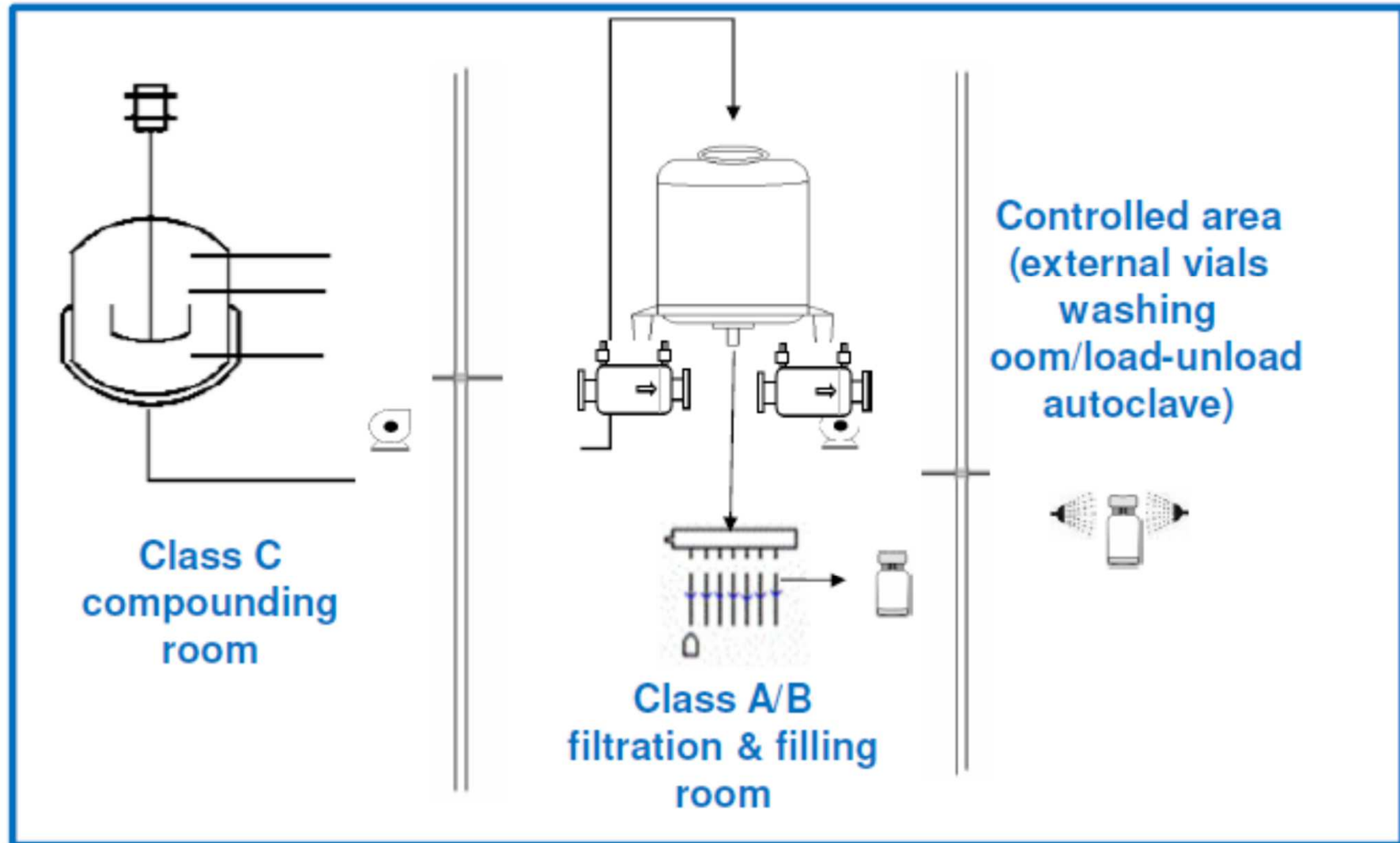
Sending site equipment

- Single Use materials used in all the production process
- Strong knowledge and recommendation to use Single Use
- No data available in the receiving unit supporting use of this new type of technology
- "Gentle" mixing needed
- Cleaning difficulties
- Difficulties in sterilizing filtration
- Preliminary compatibility data with Single Use available

Sending site equipment
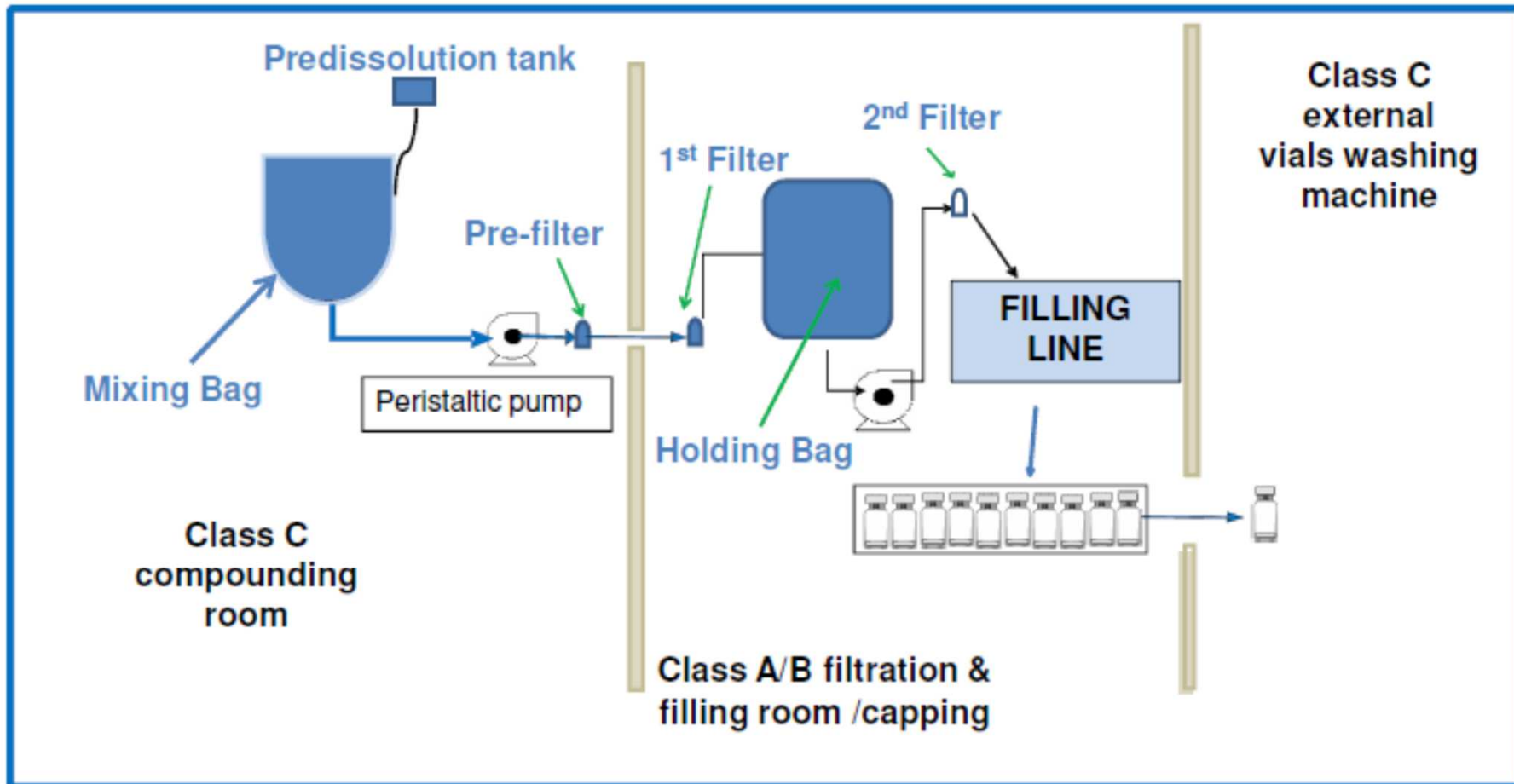
Major risks

- New technology for the receiving unit
- Challenges in some process steps to be analyzed due to partial blid TT
- Strict timelines and no possibility of mistake

Actions

- Challenge the network for similar product and similar product
- Training by suppliers and by consultants on technology
- Development plan defined and agreed with the Client to support data missed
- Execution of preliminary trials with "small scale" system before the production of technical and submission batches

Technology Transfer Workshop

Let' do exercise

pda.org

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 with several non conformity linked with product chemical characteristics.

Questions:

  Which Criteria will you use to select a new manufacturing site? List at least three main criteria

Discussion

❑**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

❑**Discussion**

❑**Background:**

Think about one Technology Transfer project you managed or you experienced

in your professional life

❑**Questions:**

    ❑Briefly describe it

    ❑Prepare a WBS

❑**Discussion**

❑**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 in US

❑ **Questions:**

❑ Divided in two groups describe the main milestones to bring the product from the SU to the RU including stage/gate and upper management main updates

❑ **Discussion**

❑**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 effort in each milestone with an "allocation diagram"

    ❑Group 2. RU Describe the project team member mainly impacted in each milestone with an "allocation diagram"

❑ **Discussion**

❑**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. Team allocation resources is completed and alignment between R and S units is in place

❑**Questions**

    ❑As RU, Design the Stakeholder Map of your TT

    ❑As SU, Design the Stakeholder Map of your TT

❑**Discussion**

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. **Brainstorm** on Stakeholders Dynamics, track them with colored lines (Influences positively, Antagonizes)

5. Design some "Action Path" to influence positively key stakeholders
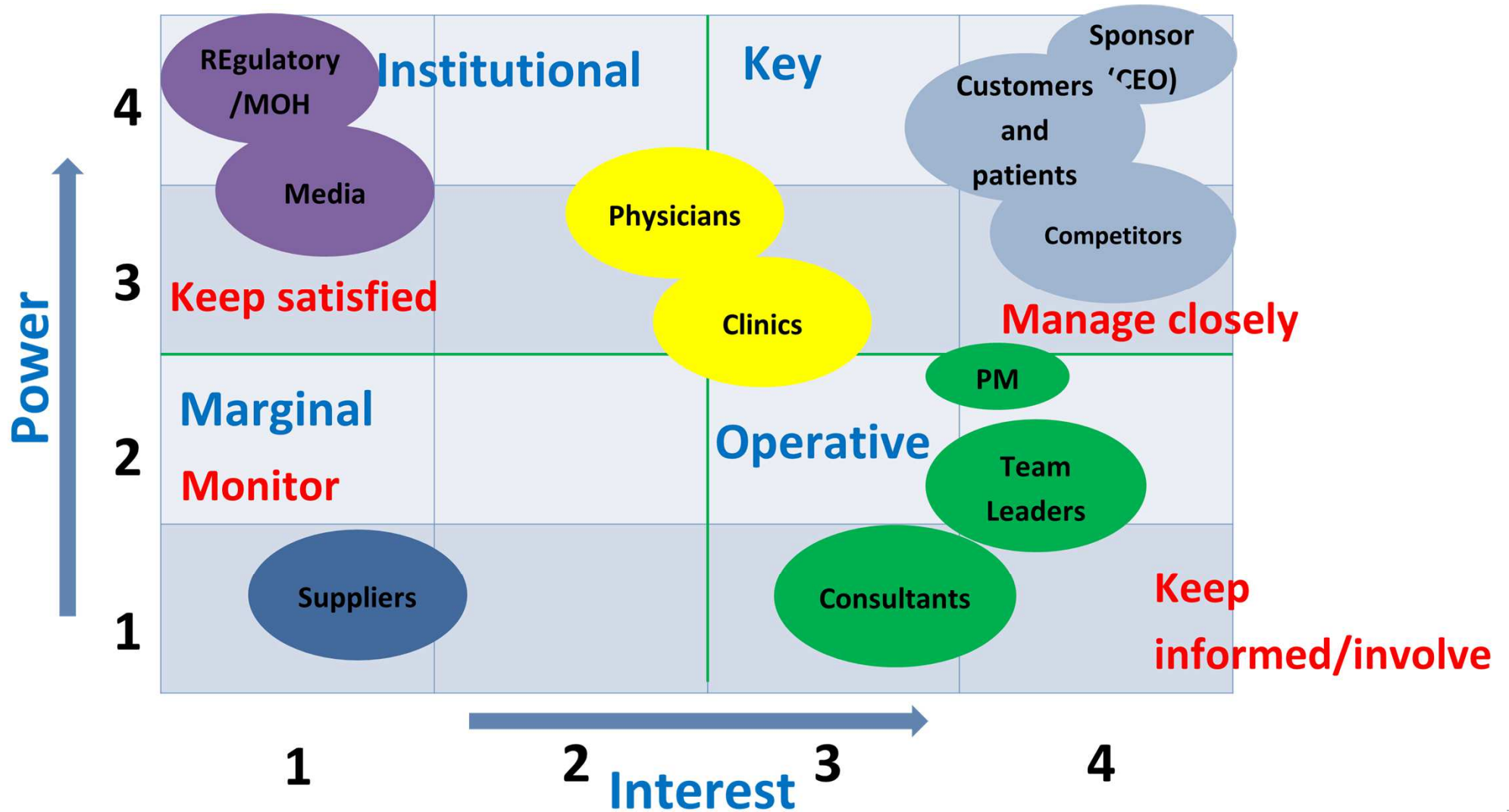
Workshop
Process transfer
case study

❑**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 for one of the phase of the process

Product	X
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
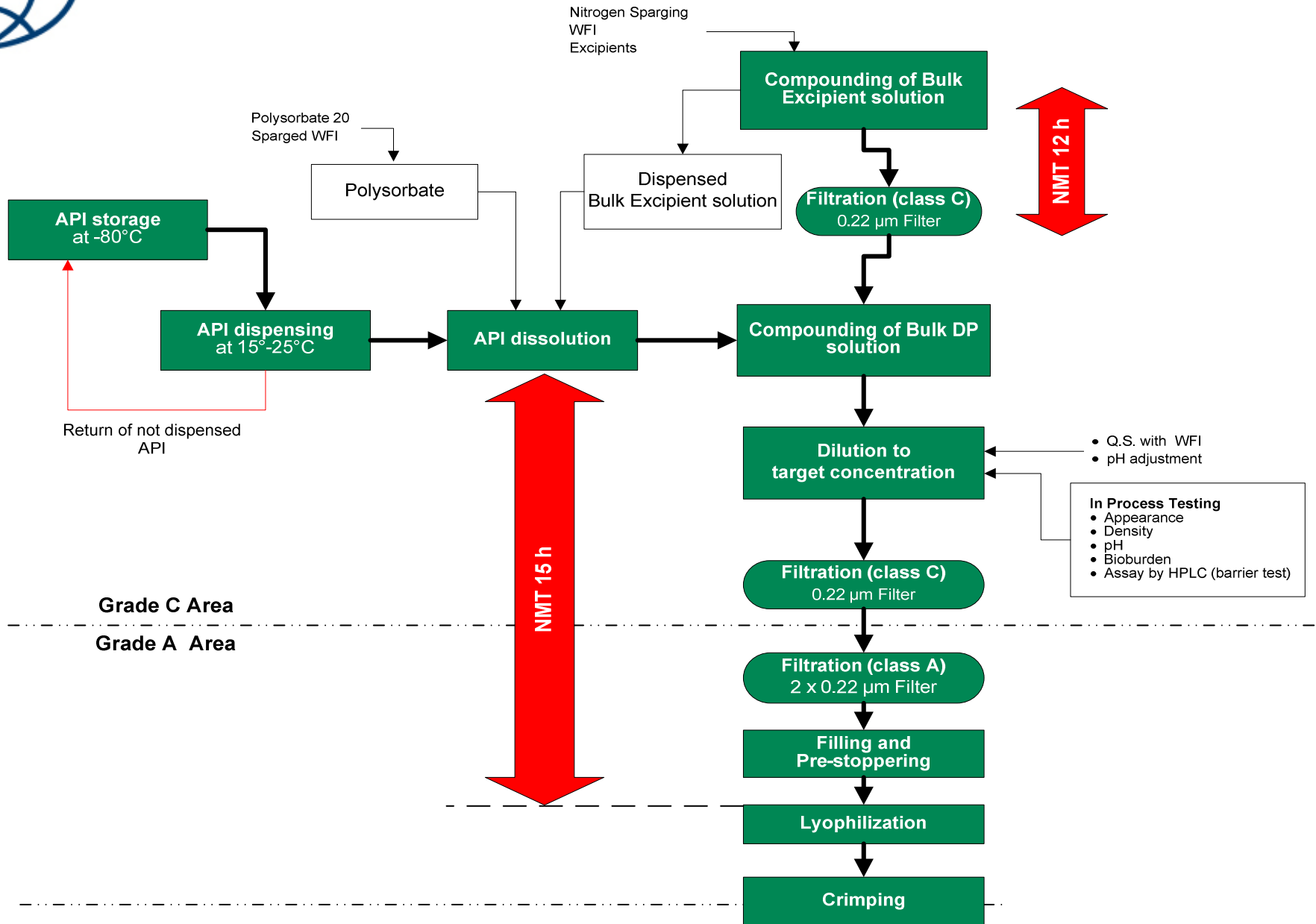
Class C

- Sparged WFI
- Excipients

Nitrogen sparging
Oxigen content: NMT 1ppm

Glass Lined Compounding Vessel CIP/SIP

Glass Carboy

Excipient solution for API dissolution

Class C

- Polysorbate
- Sparged WFI

Glass Carboy

Polysorbate Solution
Conc 1

Sparged WFI

Glass Carboy

Polysorbate Solution
Conc 2

Class C

Sincalide container

API into a dessicator
from -70°C storage

Glove Box
Nitrogen atmosphere
Analytical scale

3- Add Weighted API

Glass Carboy

Glass Carboy

Glass Carboy

1- Add Excipient solution

2- Add Polysorbate
solution

API solution
Nitrogen Purged

Class C

1- Add   API   Solution
2- Rinse with all remaining pre-dispensed excipient solution
3- Rinse with purged WFI

Glass
Carboy

4- Q.S. with WFI to final weight
5- Adjust pH if needed

Nitrogen sparging

Glass Lined
Compounding
Vessel

Class C

Class B/A

Glass Lined Compounding Vessel

Disposable line

Glass Surge Tank

Peristaltic filling pumps

Bioburden redution

0.22 µm

Redundant sterile filtration

0.22 µm   0.22 µm

Peristaltic pump

Connecting People, Science and Regulation®

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: take away from TT IG

Case studies

pda.org

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

Which is your TT RoadMap?

FEASIBILITY

KEY ACTIVITIES
- Define Project Scope
- High-level Gap & Risk Analysis
- Create Transfer Plan
- Implement Tech Transfer SOP

STAGE GATE

KEY ACTIVITIES
- Continue Risk Analyses
- Execute and Update Transfer Plan
- Train Staff

SET UP ANALYTICAL METHODS

SET UP PRODUCTION

SMALL-SCALE TRIALS

STAGE GATE

TECH BATCH

STAGE GATE

STABILITY BATCH PRODUCTION

REGULATORY PROCEDURE

APPROVAL

COMMERCIAL PRODUCTION

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)

What are the key factors for a successful Technology Transfer in your experience?

What are the main difficulties in a Technology Transfer in your experience?

Connecting People, Science and Regulation®

Conclusions

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).

Sending unit
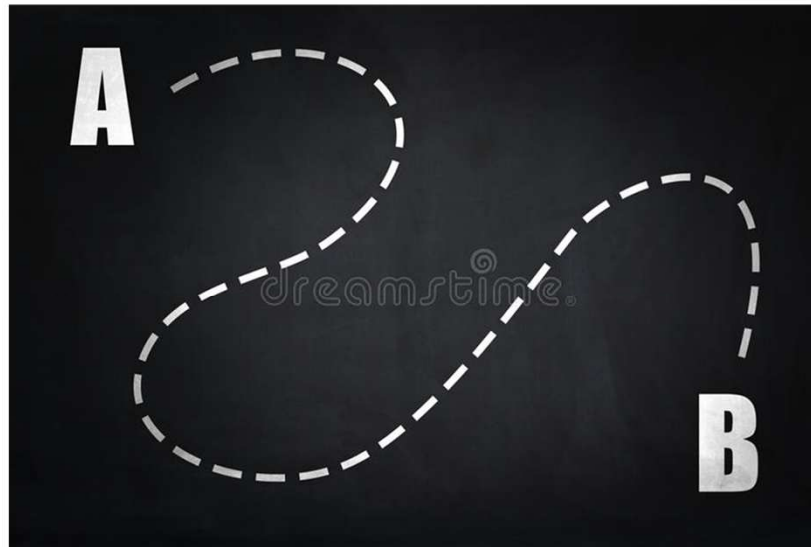
Receiving unit

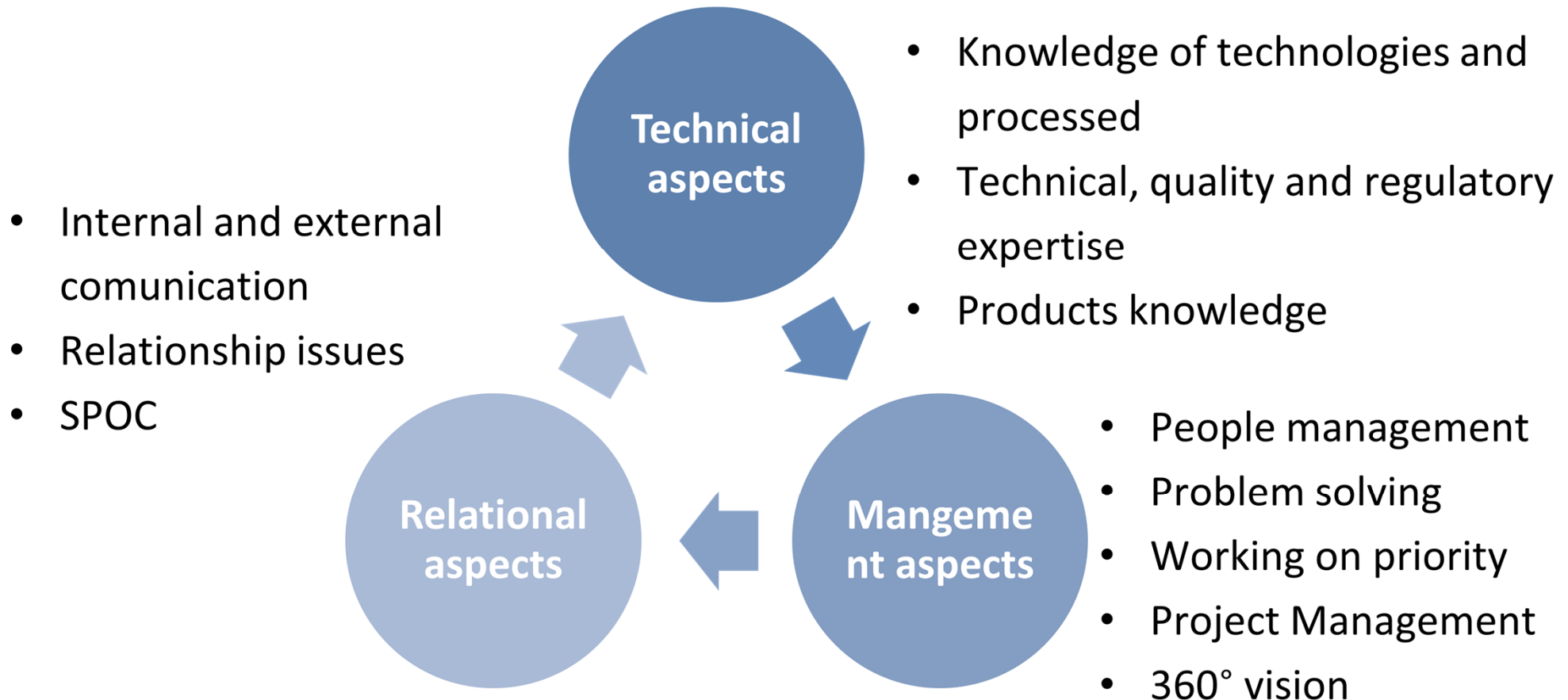*PDA – PMCO Program – Technical Report N.65*

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** is a systematic procedure that shall be executed with the aim to transfer knowledge and experience related to a pharmaceutical process from one organization to another. Technology transfer includes documentation transfer and proven ability of the receiving unit to execute what has been transferred»

Technical aspects

- Knowledge of technologies and processed
- Technical, quality and regulatory expertise
- Products knowledge

Mangement aspects

- People management
- Problem solving
- Working on priority
- Project Management
- 360° vision

Relational aspects

- Internal and external comunication
- Relationship issues
- SPOC

- Technology Transfer is not possible without a team

- Team shall be managed, organized and motivated

- Role and leadership of the PM are crucial for Technology Transfer success

- Stakeholders are different and shall be managed

PEOPLE ARE CRUCIAL FOR A SUCCESSFULL TECHNOLOGY TRANSFER

Define scope, plan, execute and track

- Project Gantt

- Action List

- Decision List

- Risk Register

- Activities completion tracking

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."

Final messages
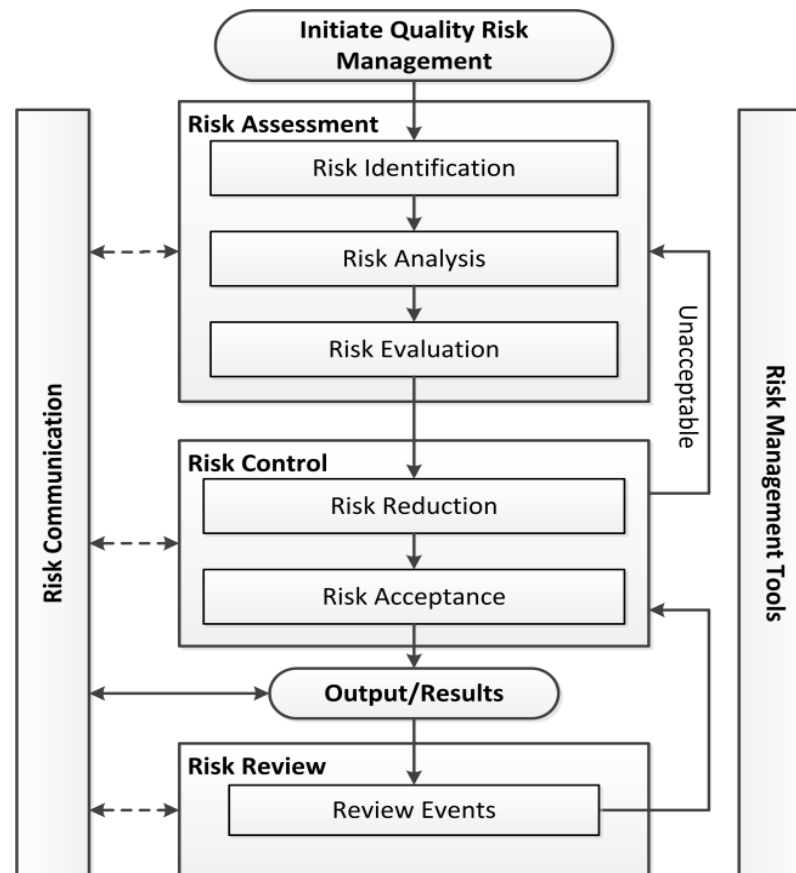
The relationship between Technology Trasfer and Project is very close: there
is no Technology Transfer without management and planning

Be prepared

Leadership is essential

Take the lead

Technical aspects are important and shall be
deeply evaluated

Devil is in the details!

Role of the people and responsibilities are crucial

Take care

Lesson learned role

Humility is a must!

Challenges are many……

Be brave!

207

Technology Transfer is a wonderful trip!

Enjoy it!

Connecting People, Science and Regulation®

Thank you!!

Angela Molaschi

a.molaschi@pharmatex.it

pda.org