Quality of learning: teaching methods

2018 EAFP Annual Conference
Experiential learning in Industry

Enrico Zambelli

Scientist, Drug Product Development Department, CMC, R&D

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People and ideas for innovation in healthcare

CONTENT

- Personal background and current working role
- Pharmaceutical industry environment: Drug process development & pharmaceutical industry organization
- Personal experiential learning: technical and soft skills acquired

PERSONAL BACKGROUND AND CURRENT ROLE

- *2006: GRADUATED IN CHEMICAL AND PHARAMCEUTICAL TECHNOLOGY AT PARMA UNIVERSITY*

  Thesis: Anti-atherosclerotic effect of Calcium antagonist agents

- *2007: RESEARCH PROJECT IN COLLABORATION BETWEEN UNIVERSITY OF PARMA AND CHIESI FARMACEUTICI FOUNDED BY SOCIAL EUROPEAN FOUND*

  "Definition of an innovative methodology for the characterization of anti-atherosclerotic drugs"

- *2007- 2018: SCIENTIST AT CHIESI FARMACEUTICI*

  2007-2009: Worked within Pharmaceutical Technology Dept. dealing mainly with pressurized Metered Dose Inhalers (pMDI) Development

  2009-2018: Working for DP Dev. Dept. (CMC) as DP Formulator Leader for several pMDI projects

  ….Personal experiential learning focused on DP development and formulation side!

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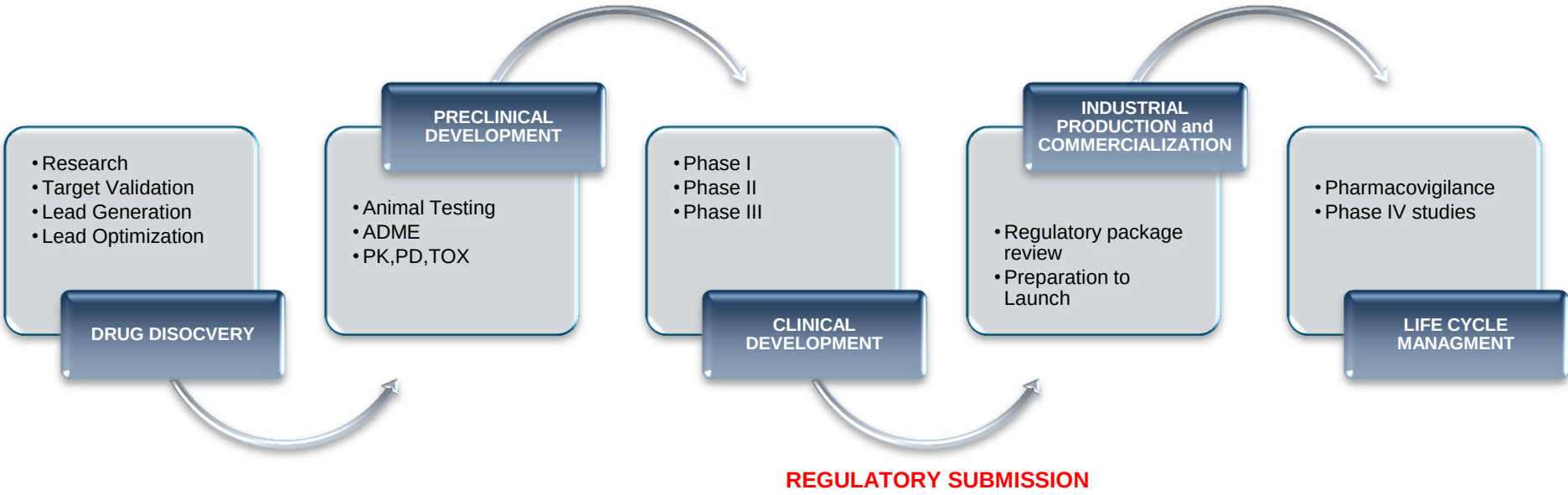
A CHALLENGING TASK…

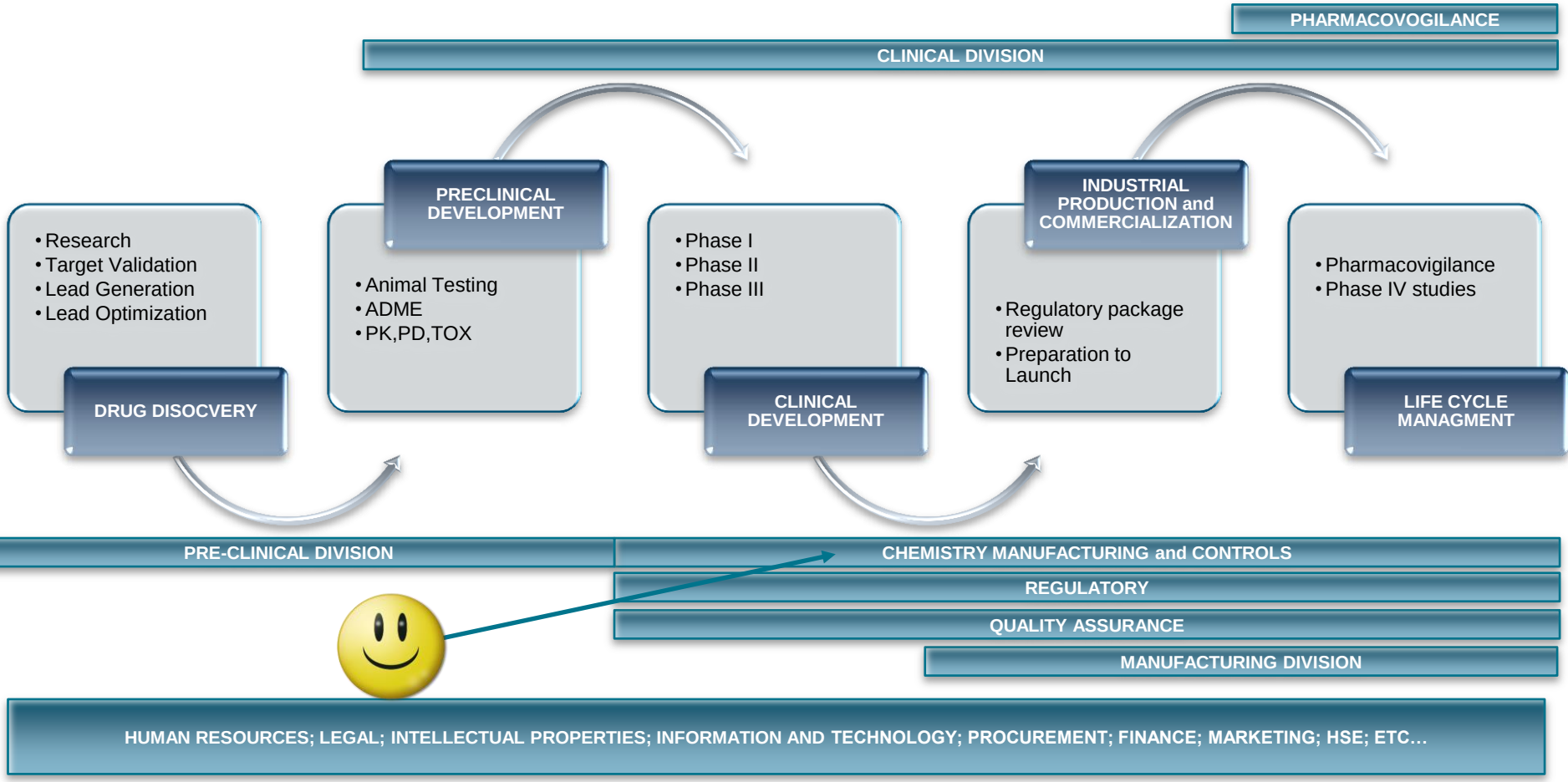
- *Drug Development Process*



- Thousands of compounds to be screened
- Many years required to reach the market (usually more than ten years for an NCE)
- High rate of failure
- Huge investment needed

…AND COMPLICATED ORGANIZATION

- *Main functional areas/divisions of pharmaceutical industry to address the drug process development*



- *The complex drug development process requires a complicated organization within the pharma industry with several interdisciplinary teams that must work together for the success*

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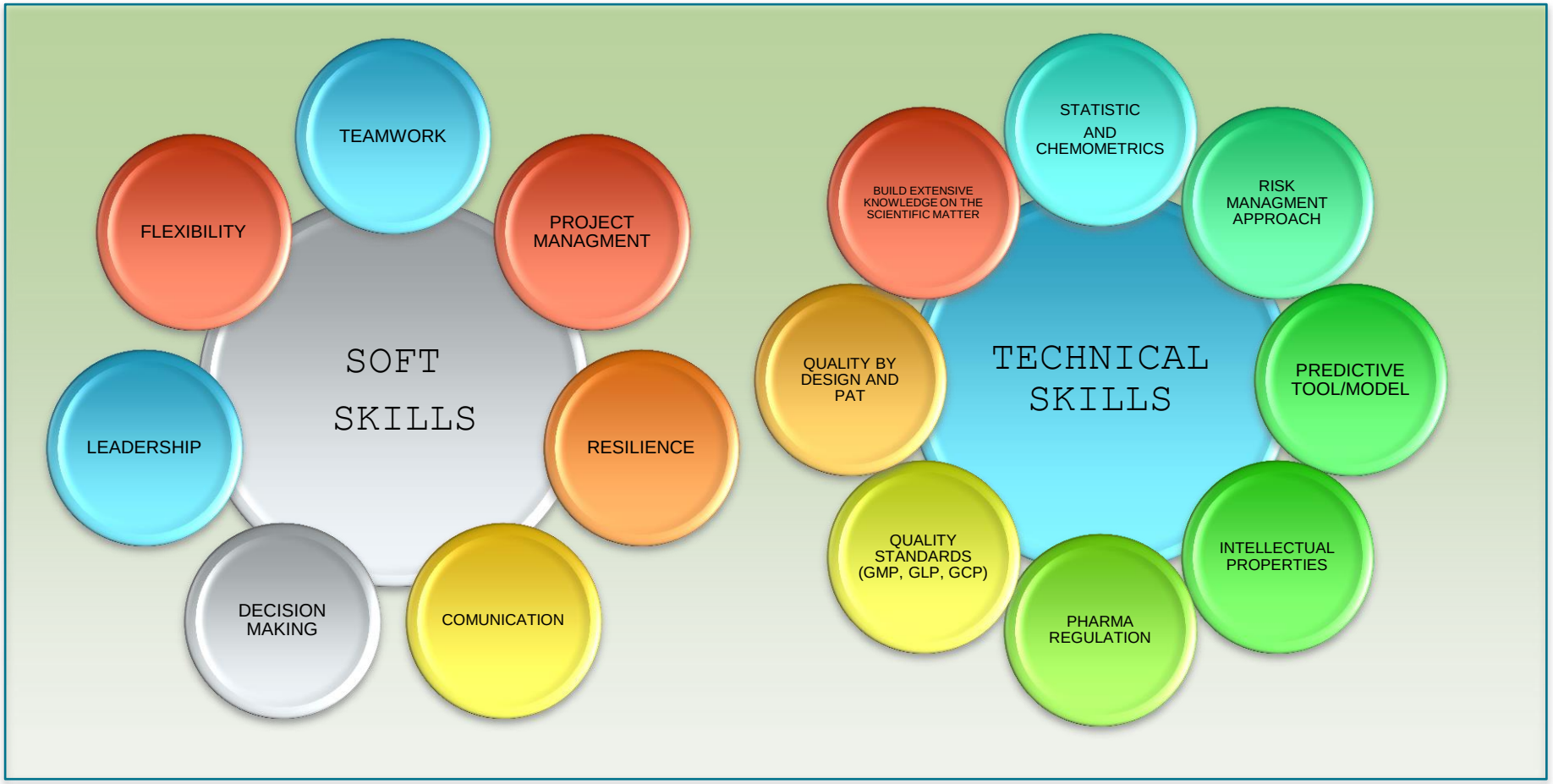
MAIN SKILLS PRACTISED WITHIN THE PHARMA INDUSTRY

Working successfully within a pharmaceutical industry requires a combination of both technical and soft skills



PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

BUILDING EXTENSIVE KNOWLEDGE ON THE SCIENTIFIC MATTER

- **Build strong knowledge on a specific and peculiar pharmaceutical form (pMDI), manufacturing process and equipment**

  - LITERATURE RESEARCH: articles, patents, exploit of company tools for specific information researches and to access to not public information

  - TRAINING and MENTORING from more experienced colleagues

  - WORKING ON THE FIELD and sharing scientific approaches , innovation and expertise among colleagues and external partners

  - PARTICULAR FOCUS ON THE PACKAGING COMPONENTS AND DEVICES REQUIRED THE UNDERSTANDING OF THE BASIS OF THE DEVELOPMENT AND PRODUCTION OF SUCH COMPONENTS (Moulding and assembly process, manufacturing process qualification, material science)

PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

STATISTIC and CHEMOMETRICS

- FROM STATISTIC TO CHEMOMETRICS: “Chemometrics is the science of relating measurements made on a chemical system or process to the state of the system via application of mathematical or statistical methods” (International Chemometrics Society definition)

- MULTIVARIATE THINKING: critical attributes and parameters of a system/process are often interacting each other so the One Variable At Time approach should be avoided.
  - Multivariate chemometrics tools: Design of Experiment (DoE), Principal Component Analysis (PCA), Partial Least Square (PLS), Multivariate Calibration

    - ADVANTAGES: full investigation of a domain defined by the investigated variables, analysis of big data set, rationalized approach to experimentation, maximization of information with less number of experiments, cost and time reduction, building of predictive tool, trusted outcomes

PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

INTELLECTUAL PROPERTIES

Patent protection encourages R&D investment and technical innovation, increasing competitiveness and economic growth

- Patents provide a negative right, or exclusivity – they provide a right to prohibit commercial efforts (production, sale, import). Exceptions: private or experimental use.

- Patents within Pharma field: API, combination of API, Formulation, Administration route, Devices, Drug products, Manufacturing process, Diagnostic…

- PATENT REQUIREMENTS:
  1. NOVELTY: new respect to the state of the art (state of the art everything publically available before the filing)
  2. INVENTIVE: not obvious for the person skilled in the art
  3. INDUSTRIAL APPLICABILITY: the invention could be reproduce at industrial level (for commercial purposes)

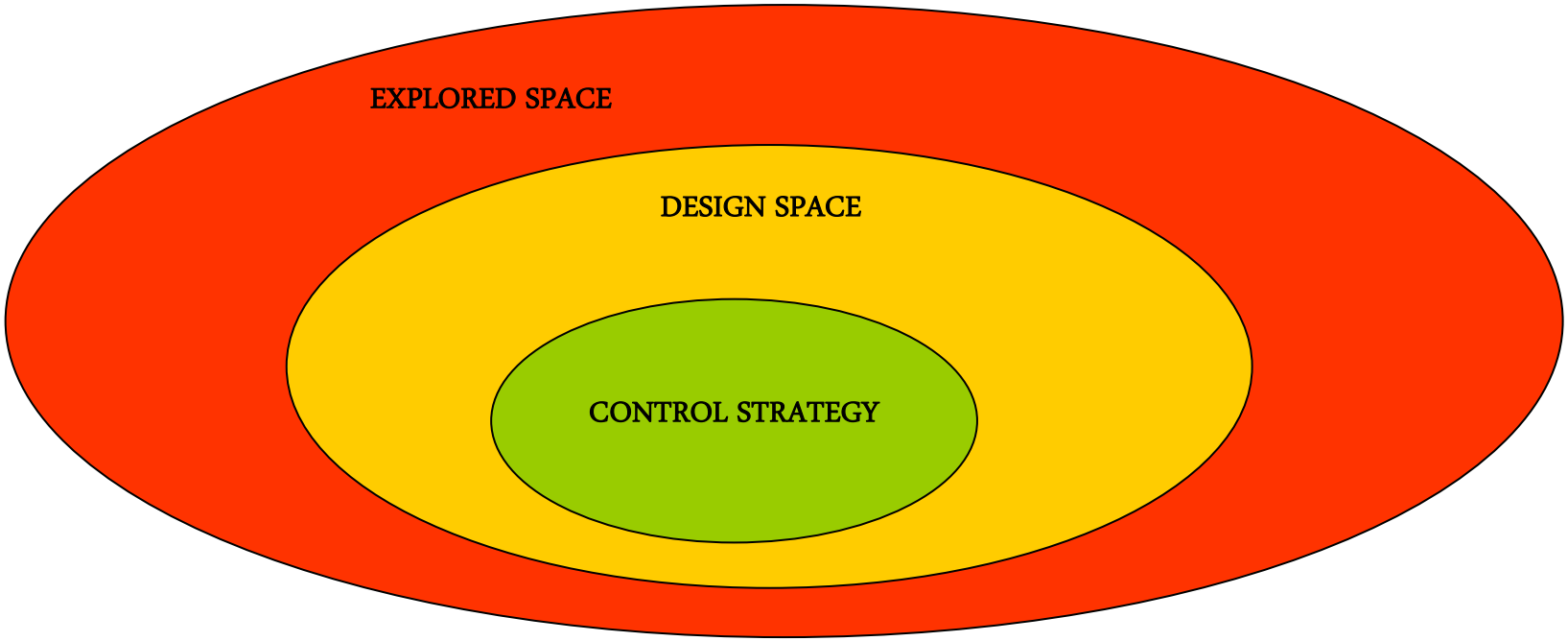
PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

QUALITY BY DESIGN (QbD)APPROACH

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management. (ICH Q8 definition)

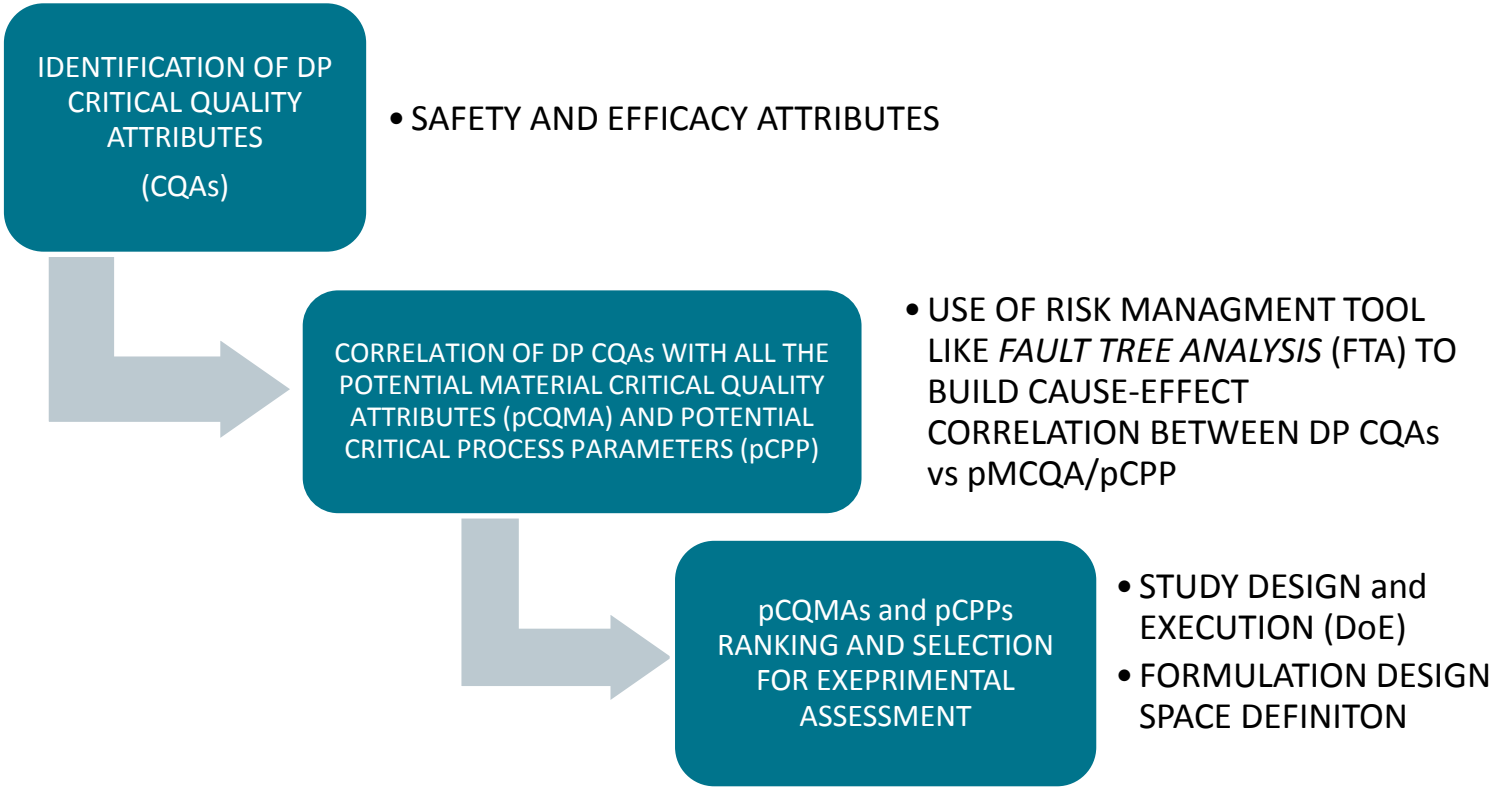
QbD relies on Multivariate Analysis tools to define the **design space** of the product were the quality of the product is assured.

PAT (Process Analytical Technology) a system of controlling manufacturing through timely measurements of critical quality attributes of raw and in-process materials. It is often used as part of a quality-by-design approach



PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

Example of QbD approach applied to DP FORMULATION DEVELOPMENT



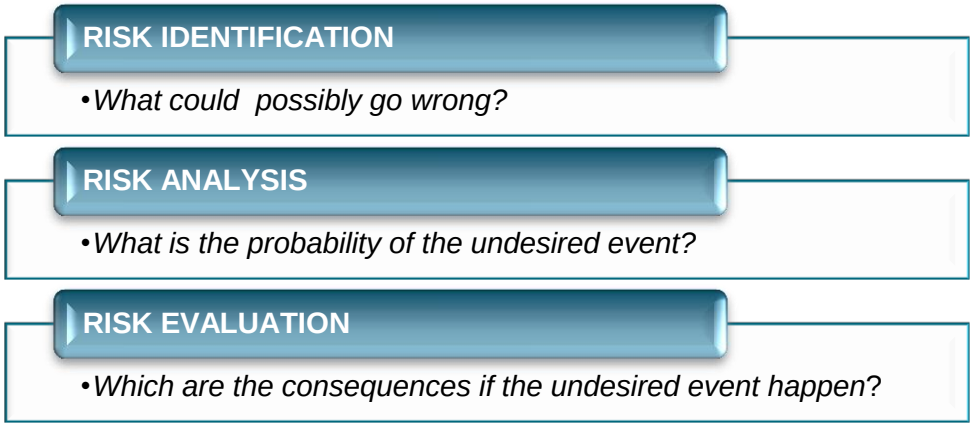
PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

QUALITY RISK MANAGEMENT APPROACH

Required for drug product development by ICH Q8 and ICH Q9, definition:

"A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle"

3 main steps 3 main questions:



For each identified risk a Risk Index is calculated (RI) as function of:

Probability x Occurrence x Severity

Probability: *based on past experience, knowledge from similar product, literature….*
Occurrence: *ability to detect the undesired event*
Severity: *impact of the event on the patient (safety & efficacy evaluation)*

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PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

PREDICTIVE TOOL and MODELING

More often the Pharma industry leverage its knowledge and its decision making process on the basis of simulation and predictive analysis especially for complex system and phenomenon where it is very difficult to obtain real data

- **CFD** (Computational Fluid Dynamics) and **DEM** (Discrete Element Method) are processes used to model or simulate systems combining fluids with solids or particles. Application of such tools on different manufacturing process steps are often used for the manufacturing process scale up as also for investigative purposes

- **MODELING** and **SIMULATION SOFTWARE** for ADMET (Absorption, Distributiuon, Metabolism, Excretion and Toxicity) prediction. Several platform are available usually specific for the desired route of administration can be very helpful in designing or modify the drug product with the aim of targeting a desired PK.

- Need to carefully evaluate and estimate the risk when decision are taken on the basis of simulation model…simulation is a simulation!!

PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

QUALITY REQUIREMENTS:

Pharmaceutical products are designed and developed in light of GOOD MANUFACTURING PRACTICE (GMP)

GMP are an essential part of the Quality Assurance system to ensure that the products are consistently manufactured to a quality appropriate to their use

Three main topics are covered by the GMP rules, corresponding to the three main chapter of Eudralex vol 4:

- Part I: covers basic requirements for medicinal products (i.e quality system, personnel, equipment, documentation, quality control, production) .
- Part II covers GMP for active substances
- Part III contains GMP related documents, which clarify regulatory expectations (Site Master File, Q9 Quality Risk Management, Q10 Note for Guidance on Pharmaceutical Quality System, etc…)

- It is essential to be able to demonstrate the quality → everything need to be documented following the GMP requirements

PERSONAL EXPERIENTIAL LEARNING: TECHNICAL SKILLS

REGULATORY REQUIREMENTS:

Regulatory requirements describes what is necessary for a new drug to be approved for marketing in a specific country or region:

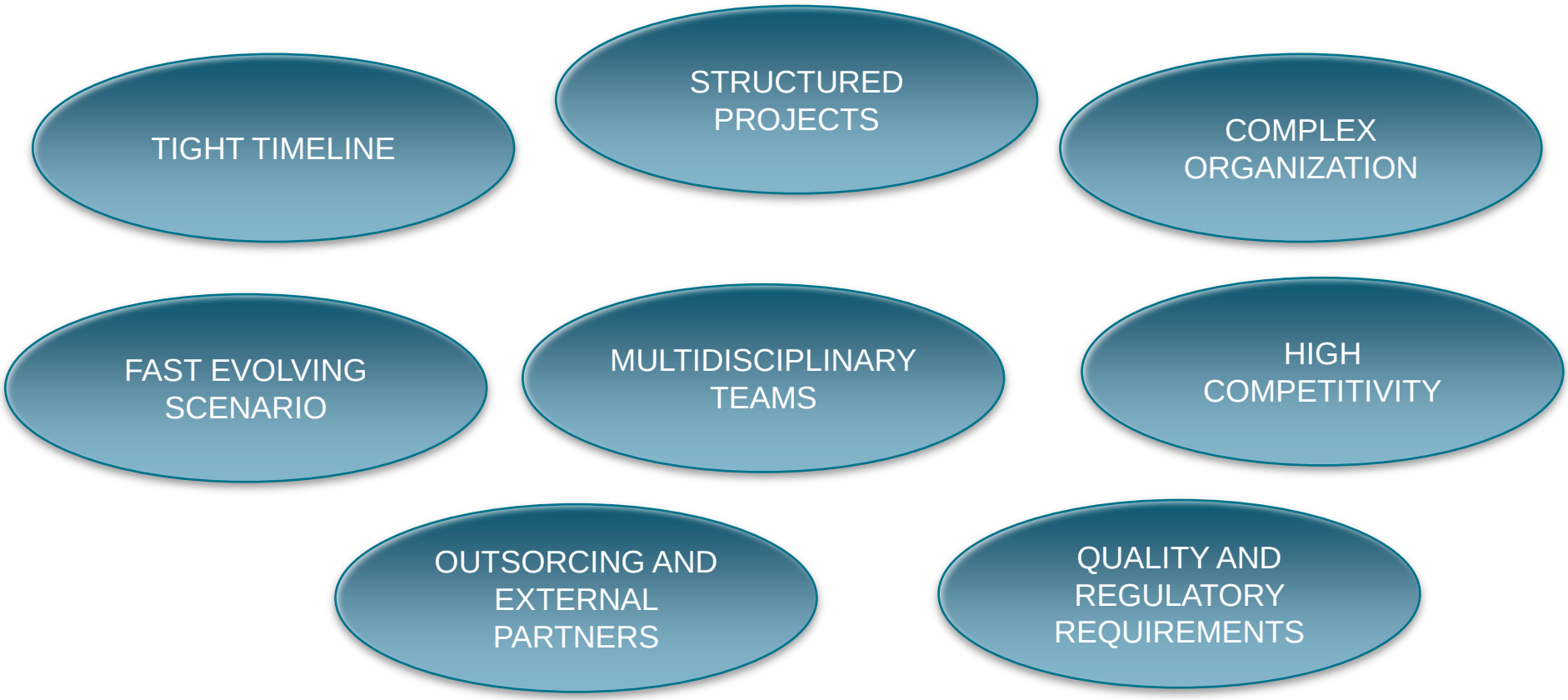
- FDA for US
- EMA for EU
- PMDA for Japan
- ANVISA for Brazil
- …
- Different authorities for different countries have different requirements which affect significantly the way of development of the drug product. This means that the DP development should be tailored for the geographical scope and the geographical scope should be clear since the beginning of the development.

- Regulatory requirements should be met since the Phase I of development and for each clinical study a specific document should be submitted and approved before the start of the trial: IMPD for EU (Investigation Medicinal Product Dossier) and IND for FDA (Investigational New Drug)

- The access to the market is regulated by the submission and approval of technical dossier: CTD for EU (Common Technical Document) and NDA for US (New Drug Application)

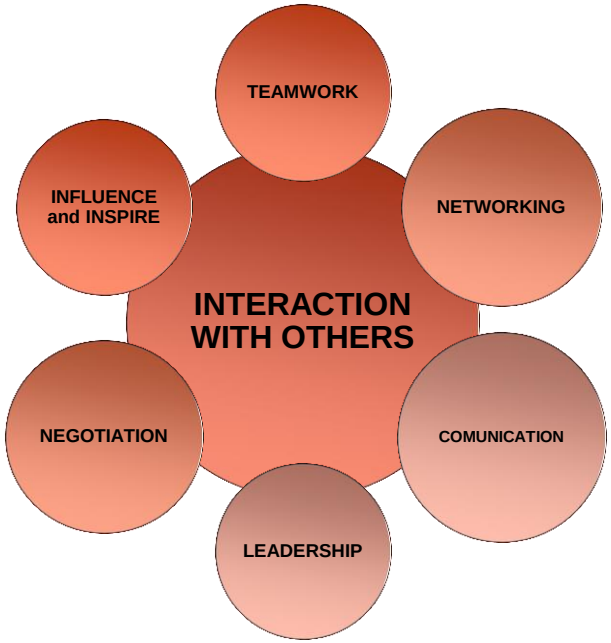
PERSONAL EXPERIENTIAL LEARNING: SOFT SKILLS

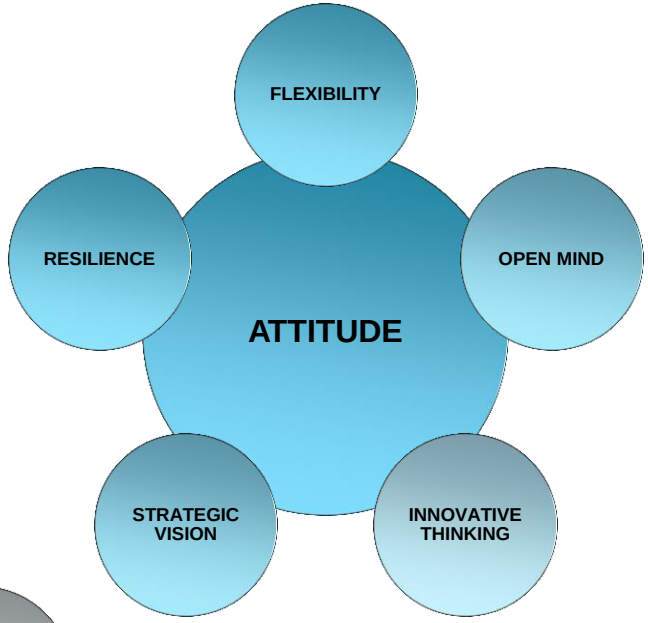
- The organization and the common way of working of the Pharma Industry requires the development and practice of specific soft skills

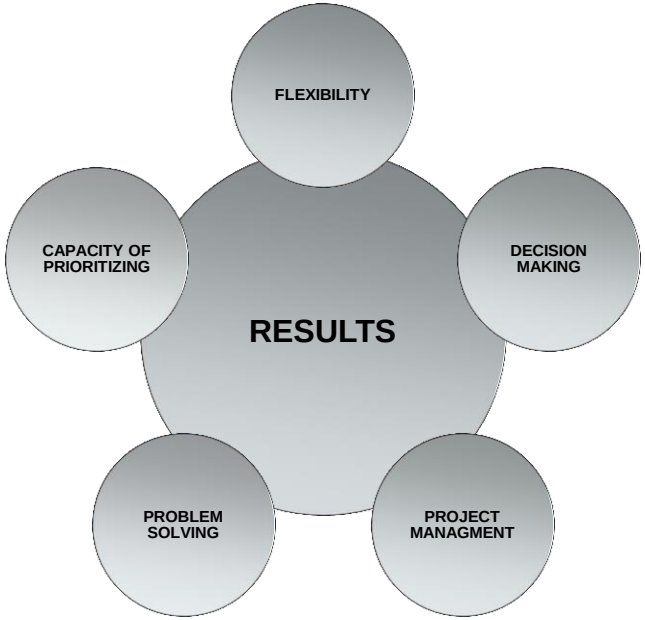


PERSONAL EXPERIENTIAL LEARNING: SOFT SKILLS

- Main soft skills practiced within the pharma industry







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