Management in Pharmaceutical Industry

Prof. Tatsiana Savitskaya
Assoc. Prof. Iryna Kimlenka

Lectures 5,6

Master Program Management: **Industrial Management**
Module: **Chemistry for Drug Substances**

The Key Aspects:

- Pharmaceutical Quality Management system
- Product Lifecycle
- Knowledge management
- The Role of Knowledge Management for New Drugs Development
- Quality Risk Management
- Managing Innovation in Pharmaceutical Industry
- Dizaster Management
- Managing Innovations

Definitions

Robert S.Kaplan, 1997

The theorem 1. 50 % of problems arise because of people, which use the same words for designation of different concepts.

The theorem 2. The rest 50% of problems arise because of people, which use the different words for designation of the same concepts.

Guidance for Industry
Center for Drug Evaluation and Research
Food and Drug Administration, April 2009 ICH
http://www.fda.gov/cber/guidelines.htm.

Pharmaceutical Quality Management System

ICH - The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.

Pharmaceutical quality system: **ICH Q10 model**

ICH Q10 describes one comprehensive model for an effective pharmaceutical quality system that is based on **International Organization for Standardization** (**ISO**) quality concepts, includes applicable **good manufacturing practice** (**GMP**) regulations, and complements **ICH** **"Q8 Pharmaceutical Development"** and **ICH** **"Q9 Quality Risk Management."** Guidance for Industry. *Center for Drug Evaluation and Research*

ICH Q10

- ✓ demonstrates industry and regulatory authorities' support of an effective pharmaceutical quality system to enhance the quality and availability of medicines around the world in the interest of public health
- ✓ Implementation of ICH Q10 throughout the product lifecycle should facilitate *innovation* and *continual improvement*

To what systems does this **Guidance** apply?

- ✓ to the systems supporting the development and manufacture of pharmaceutical drug substances (i.e., active pharmaceutical ingredients (APIs)) and drug products, including biotechnology and biological products, throughout the product lifecycle.

Product lifecycle (PL) stages

PL it is the stages a **product** goes through from when it was first thought of until it finally is removed from the market.

- The first and introduction stage is product development
- The growth stage is a period of rapid market acceptance and increased revenues that are coming in as profits.
- The maturity stage is a period where many competitors will emerge so it is important for marketers to keep their customers
- The decline stage can occur for various reasons, including advances in technology, shifts in consumer tastes, and increased competition.

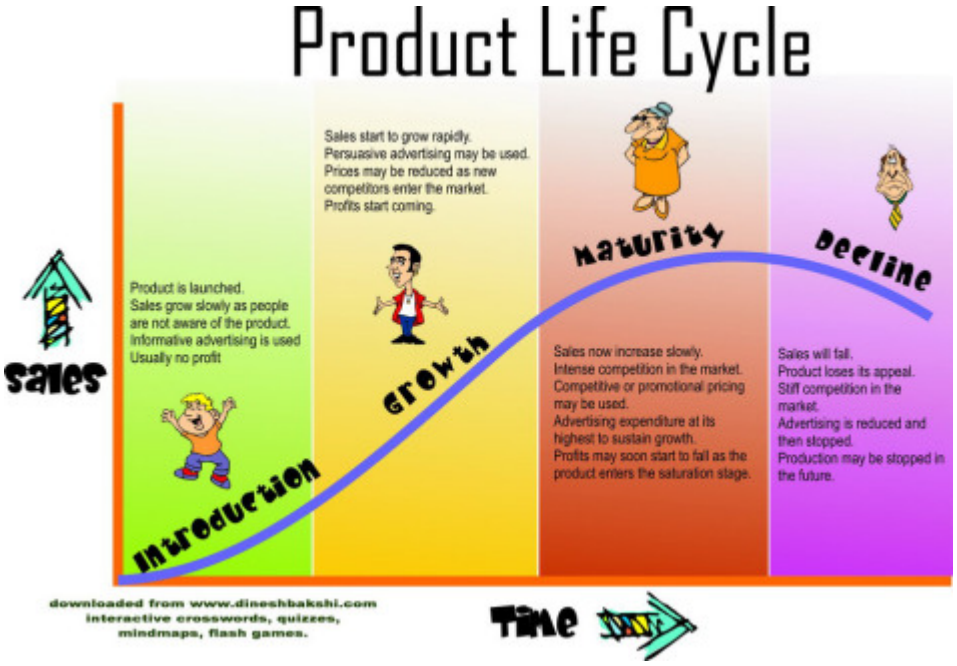
Pharmaceutical Sector Landcape:

Pharmaceutical companies around the globe continue to be buffeted by

- blockbuster drug patent expirations,
- rapidly increasing competition from generics manufacturers,
- and government and health care industry efforts to control costs — evidenced by price controls,
- pro-generics policies, and patent challenges.
- Some breakthrough branded specialty drugs (e.g., for cancer treatments and Hepatitis C treatment) can still warrant premium prices.

Product Lifecycle Activity

- **Pharmaceutical Development**
- **Technology Transfer**
- **Commercial Manufacturing**
- **Product Discontinuation**



• Pharmaceutical Development

- ✓ Drug substance development
- ✓ Formulation development (including container/closure system)
- ✓ Manufacture of investigational products
- ✓ Delivery system development (where relevant)
- ✓ Manufacturing process development and scale-up
- ✓ Analytical method development

Technology Transfer

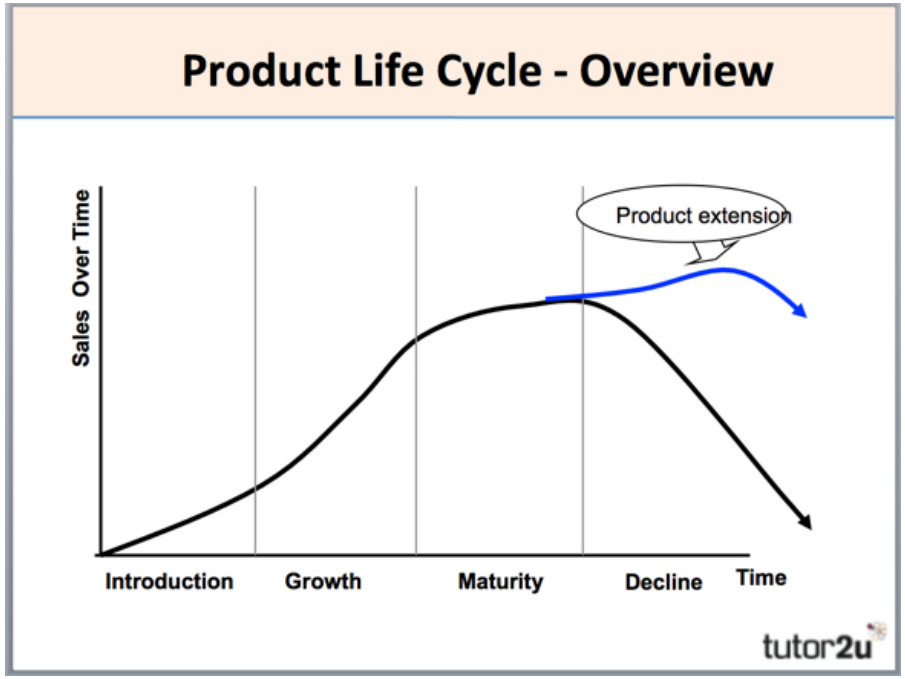
- ✓ New product transfers during development through manufacturing
- ✓ o Transfers within or between manufacturing and testing sites for marketed products

Commercial Manufacturing

- ✓ Acquisition and control of materials
- ✓ Provision of facilities, utilities, and equipment
- ✓ Production (including packaging and labeling)
- ✓ Quality control and assurance
- ✓ Release
- ✓ Storage
- ✓ Distribution (excluding wholesaler activities)

Product Discontinuation and Product Extension

- ✓ Retention of documentation
- ✓ Sample retention
- ✓ Continued product assessment and reporting



ICH Q10 Objectives

Implementation of the Q10 model should result in achievement of three main o that complement or enhance regiona requirements.

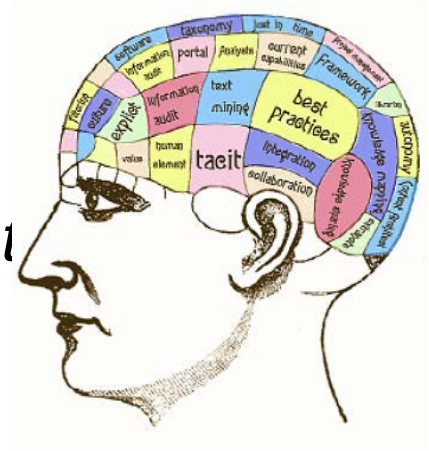
- Achieve Product Realization
- Establish and Maintain a State of Control
- Facilitate Continual Improvement

What do they need to implement product quality improvement?

- To identify and implement appropriate product quality improvements,
- Quality risk management can be useful for identifying and prioritizing areas for continual improvement.
- Use of knowledge management and quality risk management will enable a company to implement ICH Q10 effectively and successfully.

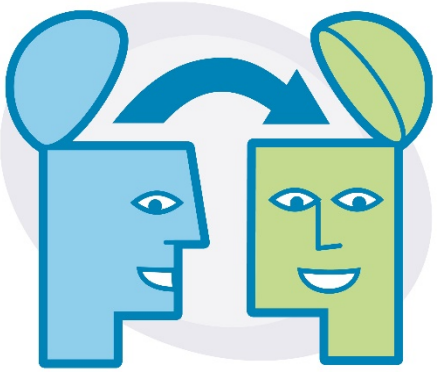
What do they need to implement product quality improvement?

- **Knowledge Management.** Knowledge management is a systematic approach to acquiring, analyzing, storing, and disseminating information related to products, manufacturing processes, and components.
- **Sources of Knowledge**: *prior knowledge* (public domain or internally documented); *pharmaceutical development studies*; *technology transfer activities; process validation studies over the product lifecycle; manufacturing experience; innovation; continual improvement; change management*



Knowledge Management

an integrated, systematic approach to identifying, acquiring, transforming, developing, disseminating, using, sharing, and preserving knowledge, relevant to achieving specified objectives.



a business philosophy. It is an emerging set of

principles, processes, organizational structures and technology applications that help people share and leverage their knowledge to meet their business

objectives.

From David Gurteen

Diversity of knowledge management definitions

- • '…*the processes that governs the creation, dissemination, and utilization of knowledge...' (Newman, 1992)*
- • '*...managing the organization's knowledge by creating, structuring, dissemination and applying it to enhance organizational performance...' (O'Leary, 1998)*
- • '…*process to acquire, organize, and communicate knowledge of employees so others may be more effective in their work…' (Alavi and Leidner,1999)*
- '…*process to acquire, organize, and communicate Knowledge (Andriessen, 2004)*

All of them are about creation, collection, preservation, sharing, spreading and usage of knowledge

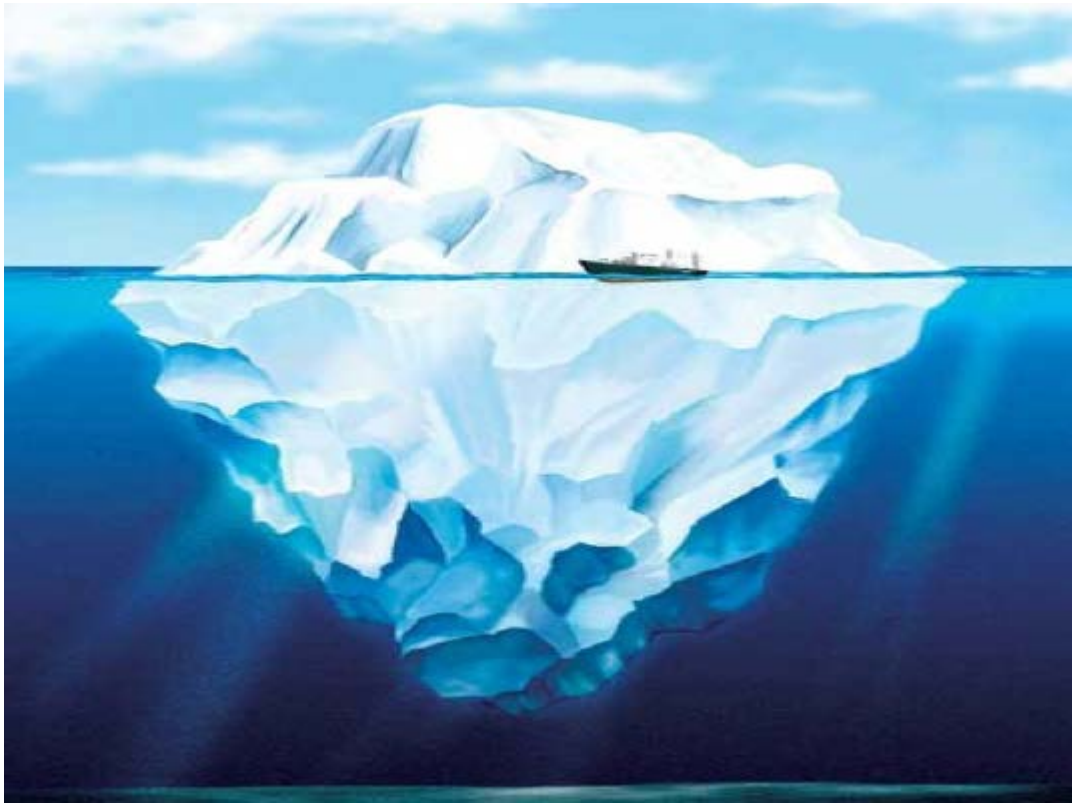
Knowledge management features

- Nowadays knowledge management (KM) practices provide companies with a competitive advantage as a result of their impact on the organization's ability to act in more efficient, sustainable and innovative ways.
- KM also influences the degree of innovativeness that a company demonstrates. It has showed by studying the way in which explicit and tacit knowledge become assets for an organization which seeks to create an adv
- The development of a knowledge sharing culture with a learning environment create opportunities for staff creativity and bright future of the company.

Metaphor of iceberg(M.Polanyi)

EXPLICIT KNOWLEDGE 20%

Documents
Information
Records
Files



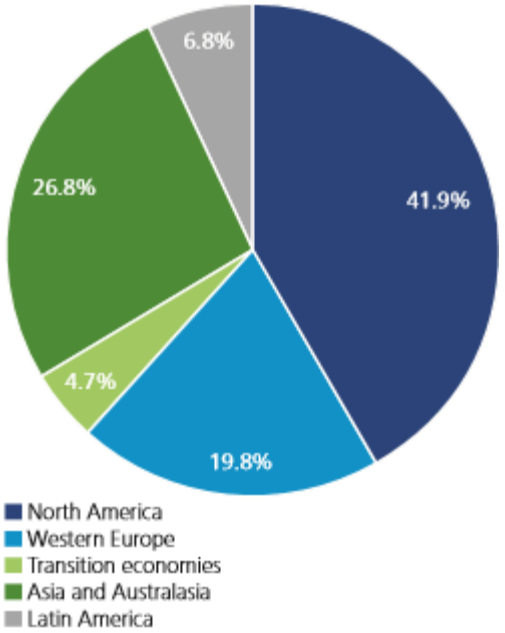
TACIT KNOWLEDGE 80%

Experience
Thinking
Competence
Commitments
Deed

IMPLICIT KNOWLEDGE

The Role of Knowledge Management for New Drugs Development

- State-of-the-art: The PI has reached $400 billion in worldwide annual sales of prescription and over-the-counter drugs.
- For thePI, innovation is often synonymous with new drug discovery and approval.
- But product innovation is getting more and more costly. Between 2002 and 2012 years, the pharma and biotech sector spent nearly $1,1 trillion on R&D.



- It costs between $800 million to $1 billion to develop a new drug and get it into the hands of consumers over a time span of 10 to 12 years

Source: DTTL Life Sciences and Health Care Industry Group analysis of *World industry outlook: Healthcare and pharmaceuticals*, The Economist Intelligence Unit, May 2014. Also, EIU database

The Role of Knowledge Management for New Drugs Development

- Strategic partnerships with universities, biotech companies, and other drug manufacturers
- Megamergers of companies such as Pfizer and Warner Lambert, Aventis, Novartis, and AstraZeneca to barrier pooling R&D potential
- Knowledge management can play an important supportive role in the challenges facing the pharmaceutical industry.

Drug Discovery - a web of processes and knowledge

New Chemical Entity (NCE)

Within each of theTherapeutic Areas the drug development process begins within the Discovery wing of the company. Here the knowledge of the employees and strategists is applied to develop compounds that are pharmacologically active against a biological target. Such initial stages of drug discovery is labelled as the development of a New Chemical Entity (NCE).

Candidate Drugs (CDs)

When a suitable NCE is forwarded within the organisation to the Clinical wing, it becomes a Candidate Drugs (CDs).

New Medical Entity (NME)

Only once a CD has passed a rigorous series of internal and external control points, trials and safety measures may the drug be released to market as a New Medical Entity (NME).

Drug Discovery - a web of processes and knowledge

- Knowledge is at the crux of drug development and the knowledge required to innovate and drive the drug discovery processes may be considered as the main asset of an organisation. Knowledge Management to all intents and purposes, would appear to be an ideal vehicle with which to reduce the amount of resource involved with the laborious process of converting a NCE to a NME.

- The top of the KM strategy:

"Personnel want to share best practices and earn from others within the company, we have to have a culture that makes it easy to share knowledge and learning"

What drives pharmaceutical innovation and knowledge exchange? aborious process of converting a NCE to a NME.

Thomas W Parsons, Thomas W Jackson & Ray Dawson. Submitted to OLKC 2006 Conference at the University of Warwick, Coventry on 20th - 22nd March 2006.

The Role of Knowledge Management for New Drugs Development

Bristol-Myers Squibb experience:

"Managing Knowledge for Competitive Advantage."

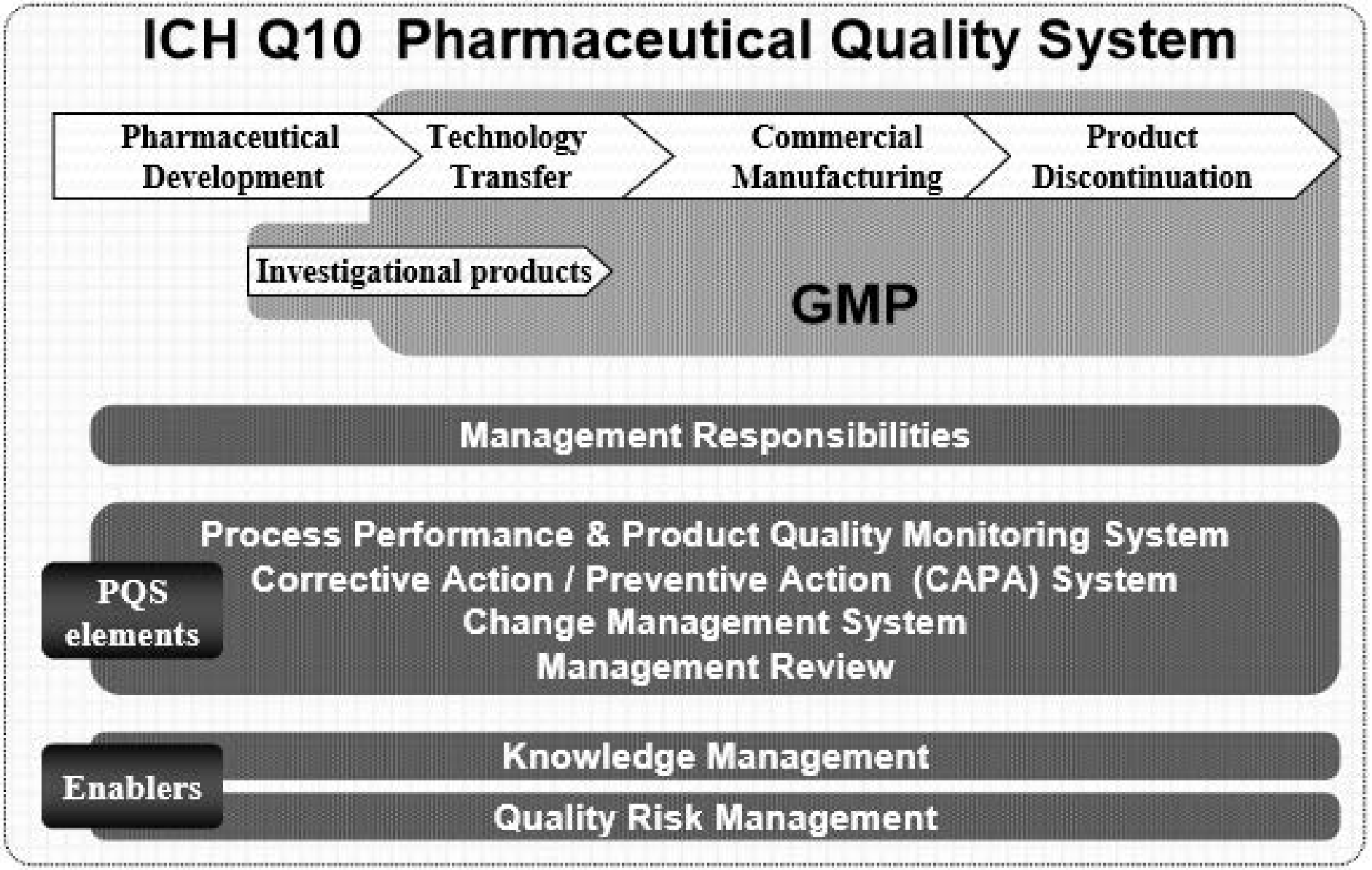
- ✓ New positions: Vice-president for knowledge management transformed to Knowledge Integrators
- ✓ Training and education of scientists to capture their own soft and hard knowledge, face-to-face exchanging knowledge,
- ✓ The goal was to turn tacit knowledge and experience into actionable learnings that can be codified, shared, and understood by a wider audience.
- ✓ They created a portal of knowledge

Bristol-Myers Squibb company experience

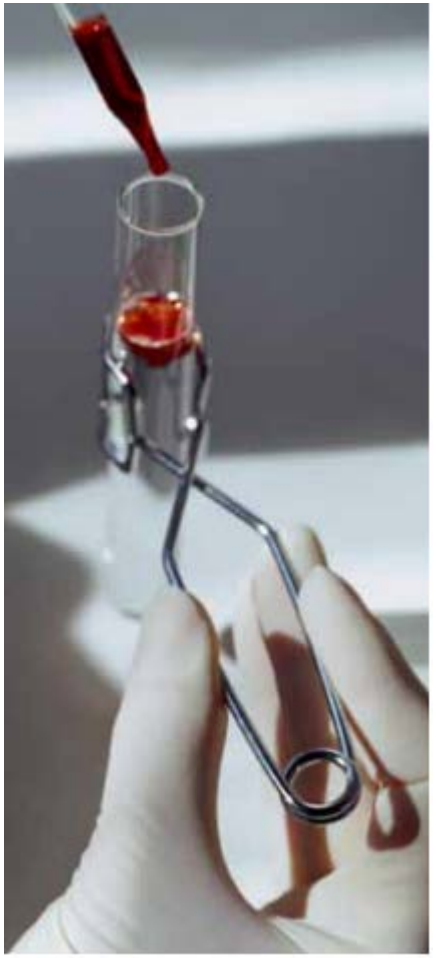
- Carla O'Dell: "The genomic revolution has unleashed a torrent of information that threatens to drown pharmaceutical firms unless they are able to know what they know, make better decisions about which molecules are the most promising, do it earlier in their discovery process, and do it faster than the co

- "My vision for Bristol-Myers is that we will eventually move to the place where we will begin to think about not just selling products, but also selling the knowledge that we've accumulated while developing our products," said Bickerstaff.

Diagram of the ICH Q10 Pharmaceutical Quality System Model



Quality Risk Management (QRM): Definitions



Risk

Combination of the probability of occurrence of harm and severity of the harm.

QRM

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

QRM: **Definitions**

- *risk assessment:* A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the evaluation of risk associated with exposure to those hazards.
- *risk control:* The sharing of information about risk and risk management between the decisionmaker and other stakeholders.
- risk evaluation: The comparison of the estimated risk to given risk criteria using a quantitative or qualitative scale to determine the significance of the risk.

QRM: **Definitions**

- *pharmaceutical product:* Any material or product intended for human or veterinary use presented in its finished dosage form or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in the exporting state and/or the importing state. pharmaceutical product
- *stakeholder* : Any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a risk. Primary stakeholders are the patient, health-care professional, MRAs and the pharmaceutical industry.

Quality Risk Management

To protect patients in terms of quality, safety and efficacy of medicines, international medicines regulatory authorities (MRAs) are recommending pharmaceutical manufacturers to adopt a risk-based approach to the life-cycle of a pharmaceutical product.

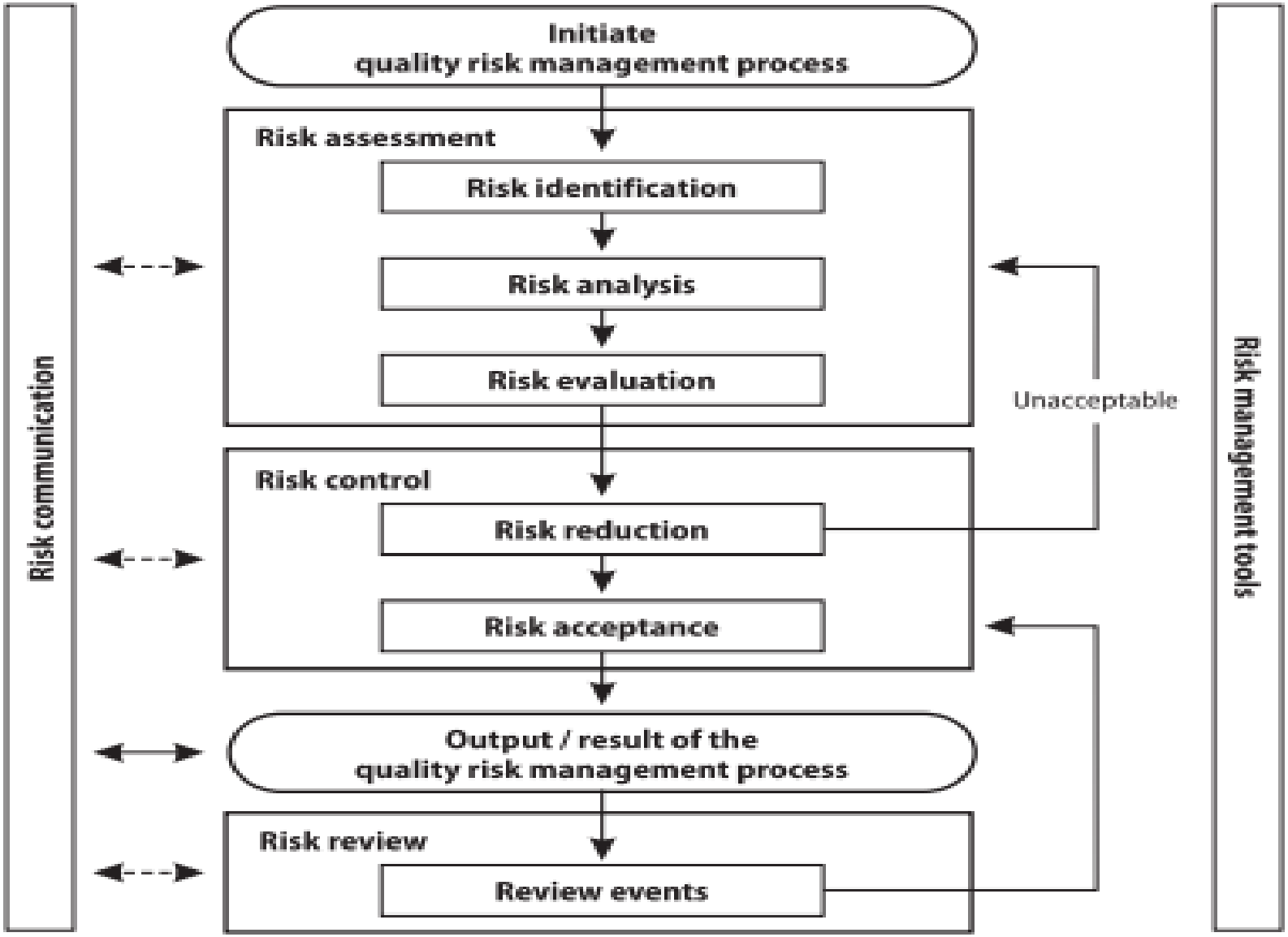
Quality Risk Management

QRM principles can be applied to both MRAs and pharmaceutical manufacturers:

– MRAs: systematic and structured planning of reviews and inspections that are risk-based. The submission review and inspection programmes can also operate in a coordinated and synergistic manner.

– Manufacturers: design, development, manufacture and distribution, i.e. the life-cycle of a pharmaceutical product. QRM should be an integral element of the pharmaceutical quality system (QS).

Overview of a typical quality risk management process



Reproduced from reference 5: ICH Q9: Quality Risk Management.

Task for the next lecture:

1. Be ready giving explanation of the QRM process according to the foregoing scheme.

Source for information:

WHO Expert Committee on Specifications for Pharmaceutical Preparations/ Annex 2 WHO guidelines on quality risk management

http://www.who.int/medicines/areas/quality_safety/quality_assurance/Annex2TRS-981.pdf