ICH Q 10 Pharmaceutical Quality System PQS

DIA China Annual Meeting, May 2010

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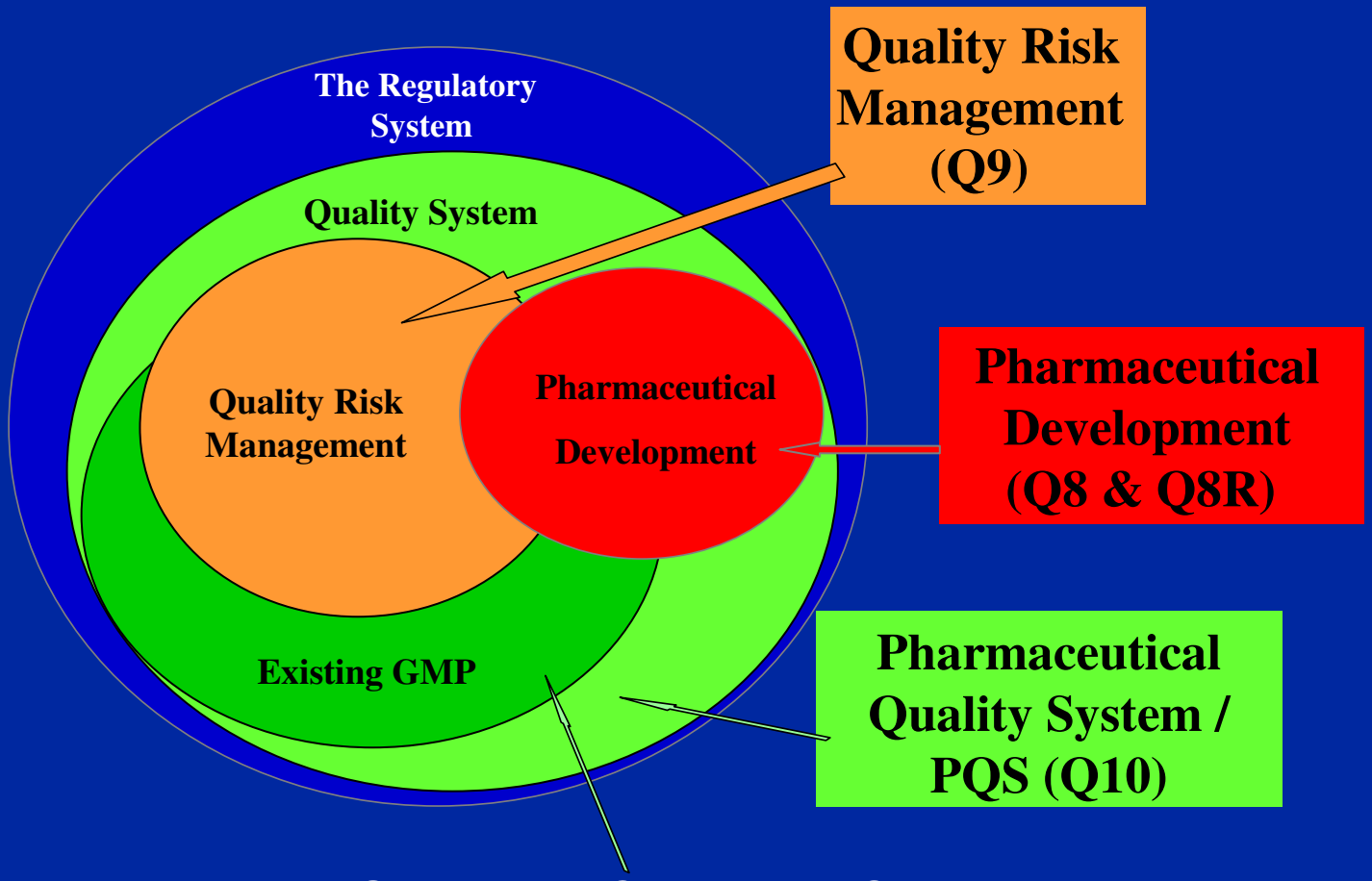
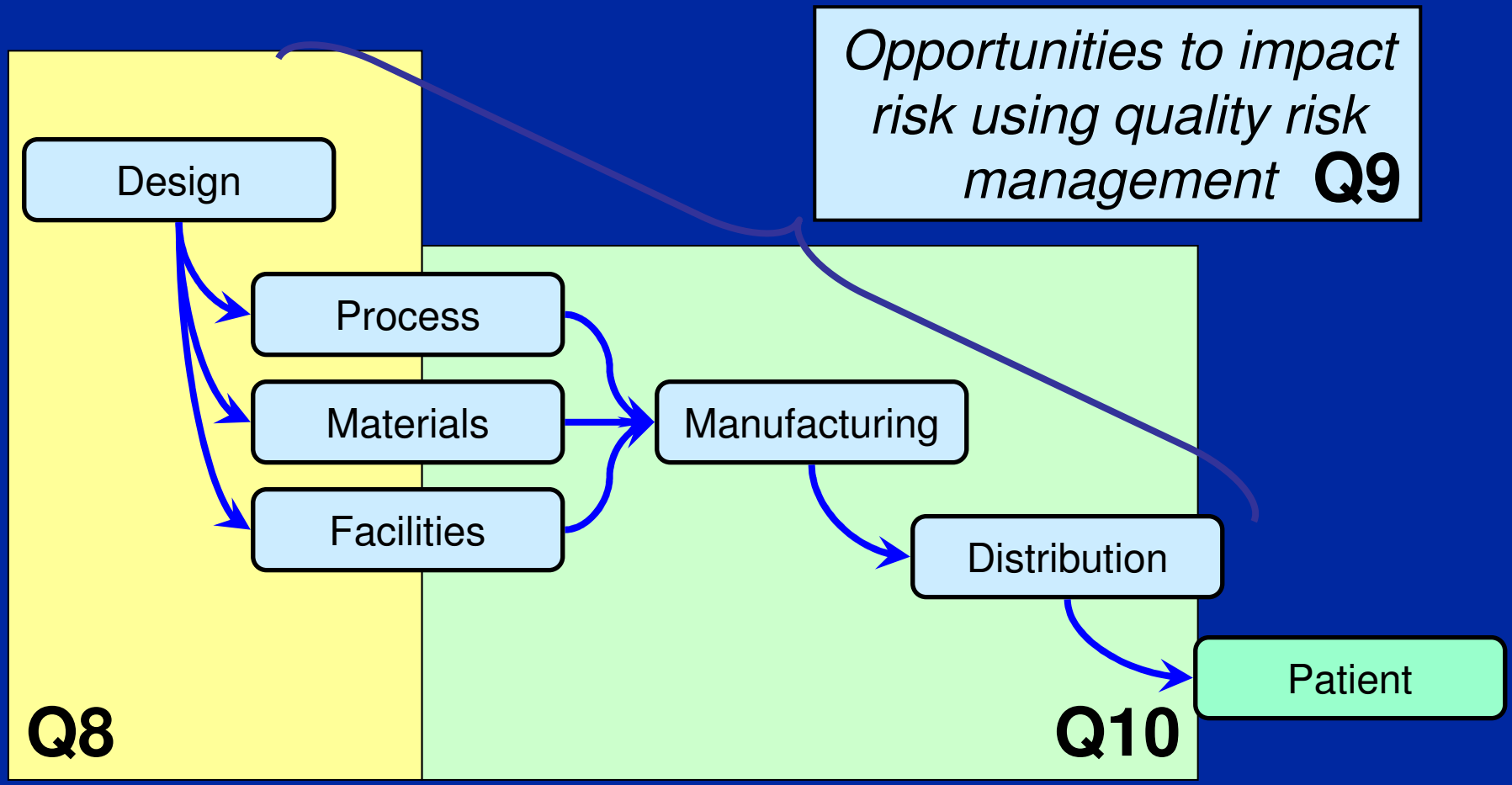
An ICH Vision for Pharmaceutical Quality

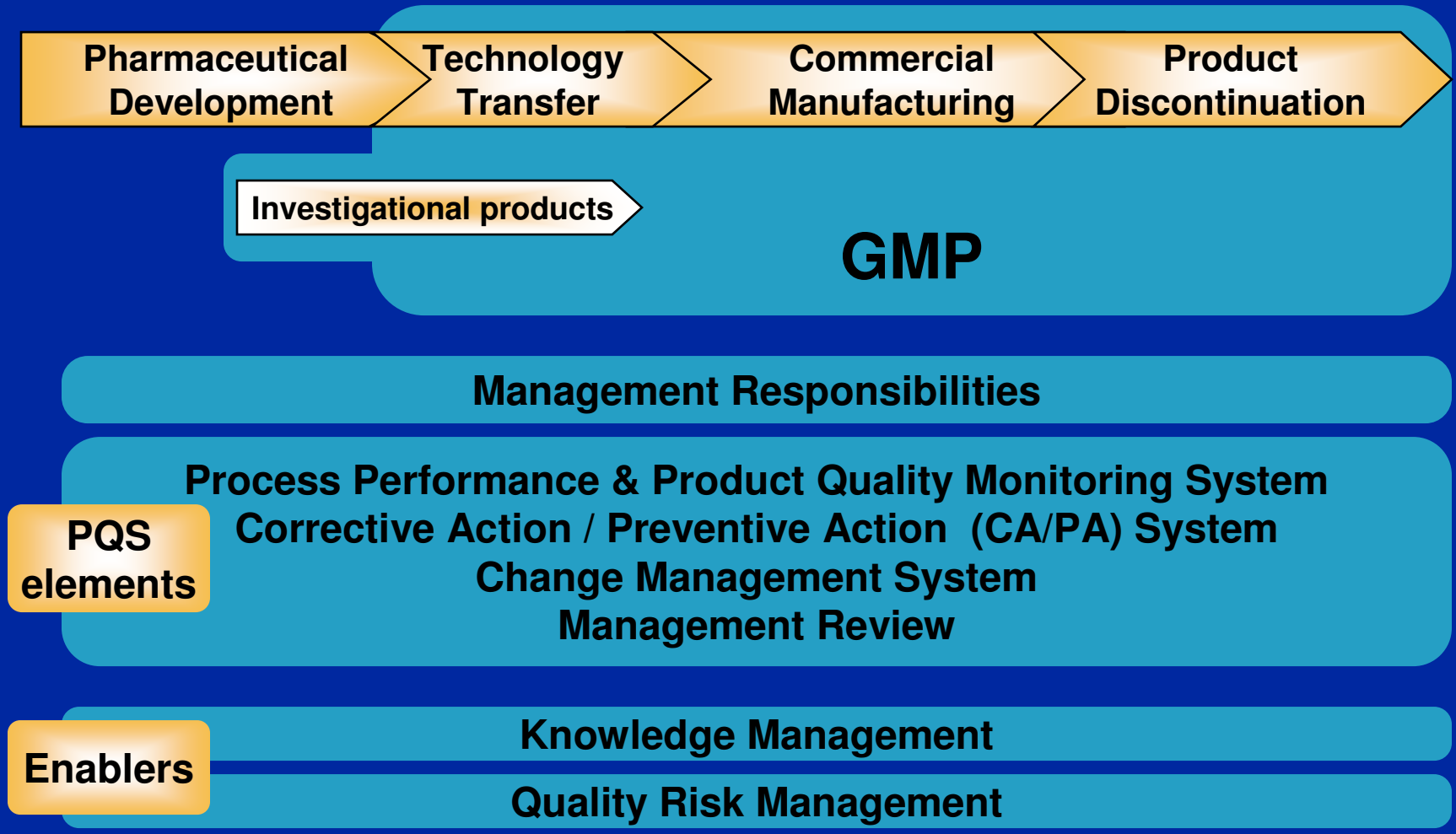


Jacques Morénas, ISPE, Nov 2007

Q9 Goal is to reduce patient risk



Q10 Pharmaceutical Quality System PQS



Q10 PQS

- Q10 encompasses the entire product lifecycle and can be applied whether or not QbD is employed.
  - Documentation
  - Training and education
  - Outsourced activities / purchased materials
  - Control Strategy
    - Use quality risk management to establish using parameters and attributes and related facility and equipment operating conditions
  - Monitoring / Handling Quality Defects (CAPA)
    - The level of effort of the investigation should be commensurate with the level of risk.
    - Result should be product and process improvements

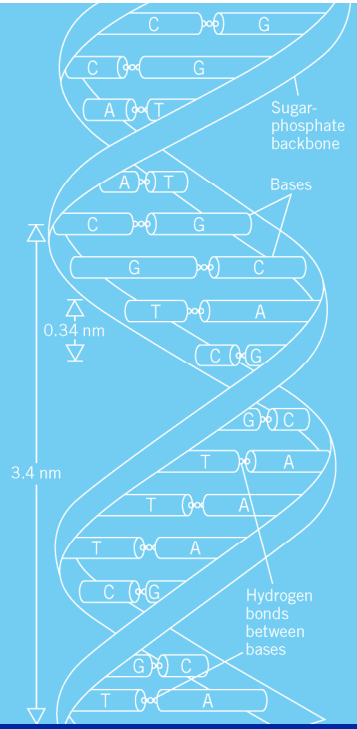
Q10 PQS

- Auditing / Inspection
  - For regulators
  - For companies
- Periodic review
- Change management / change control
  - Driven by innovation, continual improvement, the outputs of process performance and product quality monitoring, and CAPA
  - Level and formality commensurate with risk
- Continual improvement – an opportunity to optimize science- and risk-based post-approval change process

Ongoing ICH Activities

- Conclusion of ongoing topics
  - Q4B
  - Q8R
  - Q10
- Implementation
  - Q8
  - Q8R
  - Q9
  - Q10

- Development of Q11 Drug Substance guideline (chemical/biotech)
- Global Cooperation Group (GCG) bringing concepts and training internationally



Implementation in the Recently Merged Roche Genentech Organization

Quality Philosophy & Prioritization Principles

Quality Philosophy

Quality is every patient's right and every employee's responsibility. Quality provides a competitive advantage and is engrained in everything we do, from concept through continuous improvement. Because our products touch human lives, quality is the true measure of our success.

Our People

Our Patients

Our Prioritization Principles

1. Right to Operate
2. Quality Supply to Patients
3. Contribution to Target

Pharma Global Technical Operations

25 Plant Operations at 20 sites, about 12 500 employees

PLUS: Over 200 contract mfg org (CMOs)

Implementation of Modern Quality Systems

- Why One Pharmaceutical Quality System (PQS)?
  - Health Authority Requirements & Standardization
  - LEAN Quality Process Expectations
  - One Company…One PQS
  - Network Wide Integrated with the Business
  - Knowledge Management
  - Reduce Product & Patient Risk
  - Drive Down Costs

Implementation of Modern Quality Systems

- What are some of the methods used:
  - Systematic implementation of Global Quality Requirements
  - End to End Product Quality Management (PQM)
  - Quality Reporting to Quality (Q2Q) across the network
  - Integration of activities across disciplines manufacturing, technical development, clinical
  - 3rd party manufacturing oversight / risk based rigor
  - Governance Structures and reporting mechanisms such as Quality Councils to Communicate and Make Decisions
  - Proactive compliance risk assessment and control as an ongoing proactive activity e.g. inspection readiness
  - Independent audit and inspection management units

Implementation of Modern Quality Systems

- *Objective/Intent*
  - Deliver an End to End (E2E) view of product quality for all Commercial products

  Critical to:
    - maintaining quality supply to patients
    - product consistency across sites
    - our right to operate
  - End to End means that the product quality:
    - is managed throughout the product value stream
    - includes both API and drug product
    - is managed throughout Product Life Cycle (Q10 enabler- Process Performance and Product Quality Monitoring)
  - Success requires knowledge transfer from Clinical to Commercial

- **PQM model captures significant synergies:**
- **Aligning the organization across the supply chain, from raw**
- **materials to distribution, for product and process lifecycle**

- Product Quality Management (Product Stewart Model)

Implementation of Modern Quality Systems

- Product Quality Management Responsibilities
  - Oversee product complaint data & management, trending, metrics and required alert reports to regulators Field Alert Reports and Biologic Product Defect Reports (FARs, BPDRs), Confirmed Complaints Issue Management
  - Responsible for QC business systems supporting QC testing network
  - Analytical methods management - perform commercial methods & product specification lifecycle management
  - Oversee Analytical Method innovation identification & implementation
  - Global assay method transfer management & method monitoring
  - Perform annual product quality assessments & data trending (APR/PQR)
  - Provide Quality product support through Product Stewards
  - Oversee Raw Materials & Stability Program Management

Implementation of Modern Quality Systems

Product Quality Management Benefits

- Dedicated resources overlooking each product to assure quality integrating activities:
  - across all sites (Mfg, QC, QA, etc)
- Single point of contact between
  - from raw materials to distribution
  - across all technical disciplines Quality and the rest of the organization
- Structured approach to knowledge management (ICH Q10 enabler) and facilitates Quality by Design
- Early warning for product quality issues
- Focused Product network
- Quality improvement activities are implemented across the network

Remaining Challenges

- Still exist and we all understand the consequences. For example:
  - adulterated materials in the supply chain causing the manufacture of poor quality products in some cases serious injuries and deaths
  - recalls causing product shortages
- Implementation of Modern Quality Systems in line with the ICH Quality Vision is needed to prevent of these serious consequences and to assure quality supply needed for patients.

Potential Opportunities to Enhance Science and Risk Based Regulatory Approaches

Scenario	Potential Opportunity
1. Comply with GMPs	Compliance – status quo
2. Demonstrate effective pharmaceutical quality system, including effective use of quality risk management principles (e.g., ICH Q9 and ICH Q10).	Opportunity to: o increase use of risk based approaches for regulatory inspections.
3. Demonstrate product and process understanding, including effective use of quality risk management principles (e.g., ICH Q8 and ICH Q9).	Opportunity to: o facilitate science-based pharma. quality assessment; o enable innovative approaches to process validation; o establish real-time release mechanisms.
4. Demonstrate effective pharmaceutical quality system and product and process understanding, including the use of quality risk management principles (e.g., ICH Q8, ICH Q9 and ICH Q10).	Opportunity to: o increase use of risk-based approaches for regulatory inspections; o facilitate science-based pharma. quality assessment; o optimise science and risk-based post-approval change processes to maximise benefits from innovation and continual improvement; o enable innovative approaches to process validation; o establish real-time release mechanisms.

Opportunities for Global Implementation

- Less reliance on testing more reliance on a manufacturer's capabilities
- Better understanding of a company's capability and profile across a global network i.e. more assurance by regulators of consistent processes and global implementation
- Companies can provide more assurance site to site for producing consistent products and analytical procedures in a global network environment
- Enhanced ability for regulators to leverage shared assessments, inspections based on common standards globally for new products, changes, and site transfers