Implementation of Q8, Q9 & Q10

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International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH Quality vision statement, Brussels July 2003

Develop a **harmonised pharmaceutical quality system** applicable **across the life cycle** of the product emphasizing an integrated approach to **quality risk management** and **science**

- Before Brussels
- Q10 background
- Real life experience :Efpia / EMEA PAT TEAM in IRELAND, April 07
- During Brussels

Implementation Working Group for ICH Q8,9 &10 Before Brussels

Decided to have a IWG in ICH Yokohama, Nov. 2007

First meeting in Portland (USA) in June 2008

- Drafting questions
- Identifying topic for interest

Between Portland & Brussels

- Established regional working groups involving observers
  - North America: Quality by Design topics
  - Japan: Knowledge Management
  - Europe: Pharmaceutical Quality Systems (PQS)
- Draft Q&A and documents prepared
- Comments discussed at teleconference
- Revision before coming to Brussels

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This diagram illustrates the major features of ICH Q 10, Pharmaceutical Quality System (PQS)

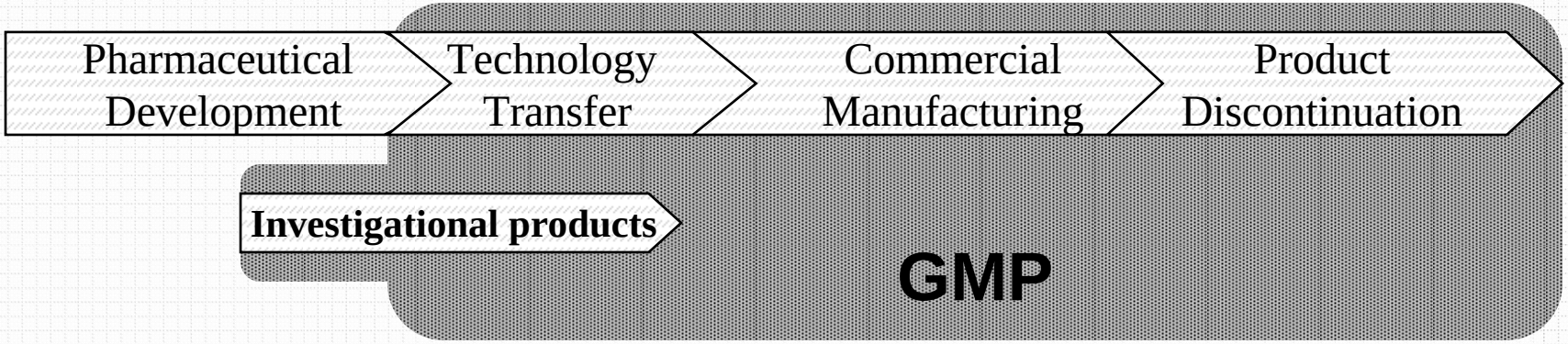
ICH Q10 Pharmaceutical Quality System

The PQS covers the entire lifecycle of a product including :

ICH Q10 Pharmaceutical Quality System

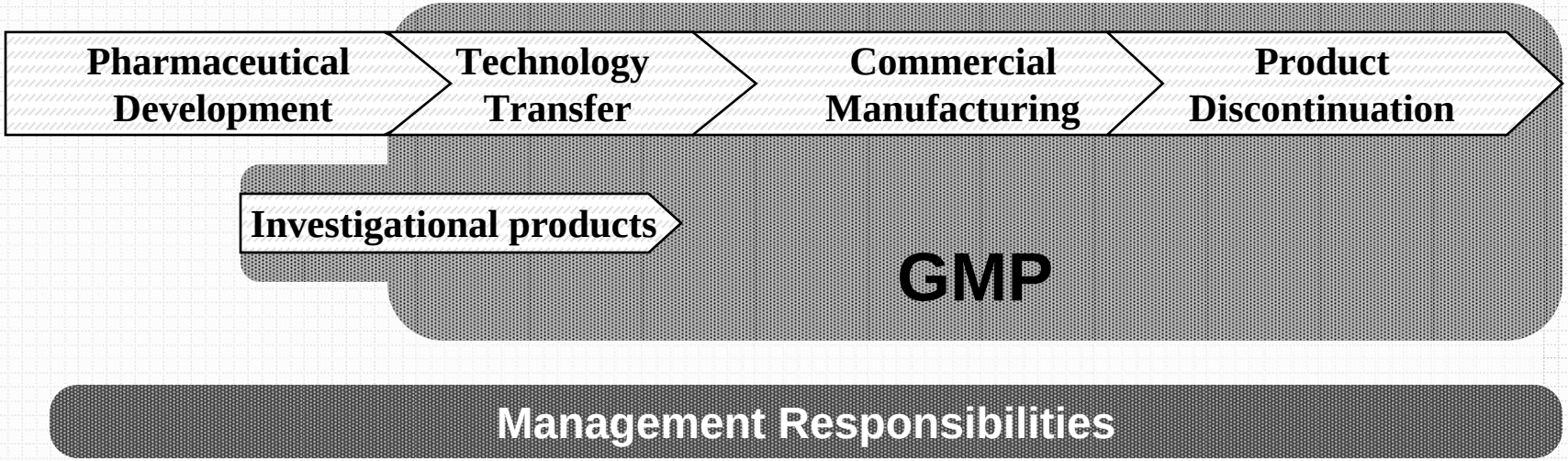
The PQS extends beyond and augments GMPs

ICH Q10 Pharmaceutical Quality System



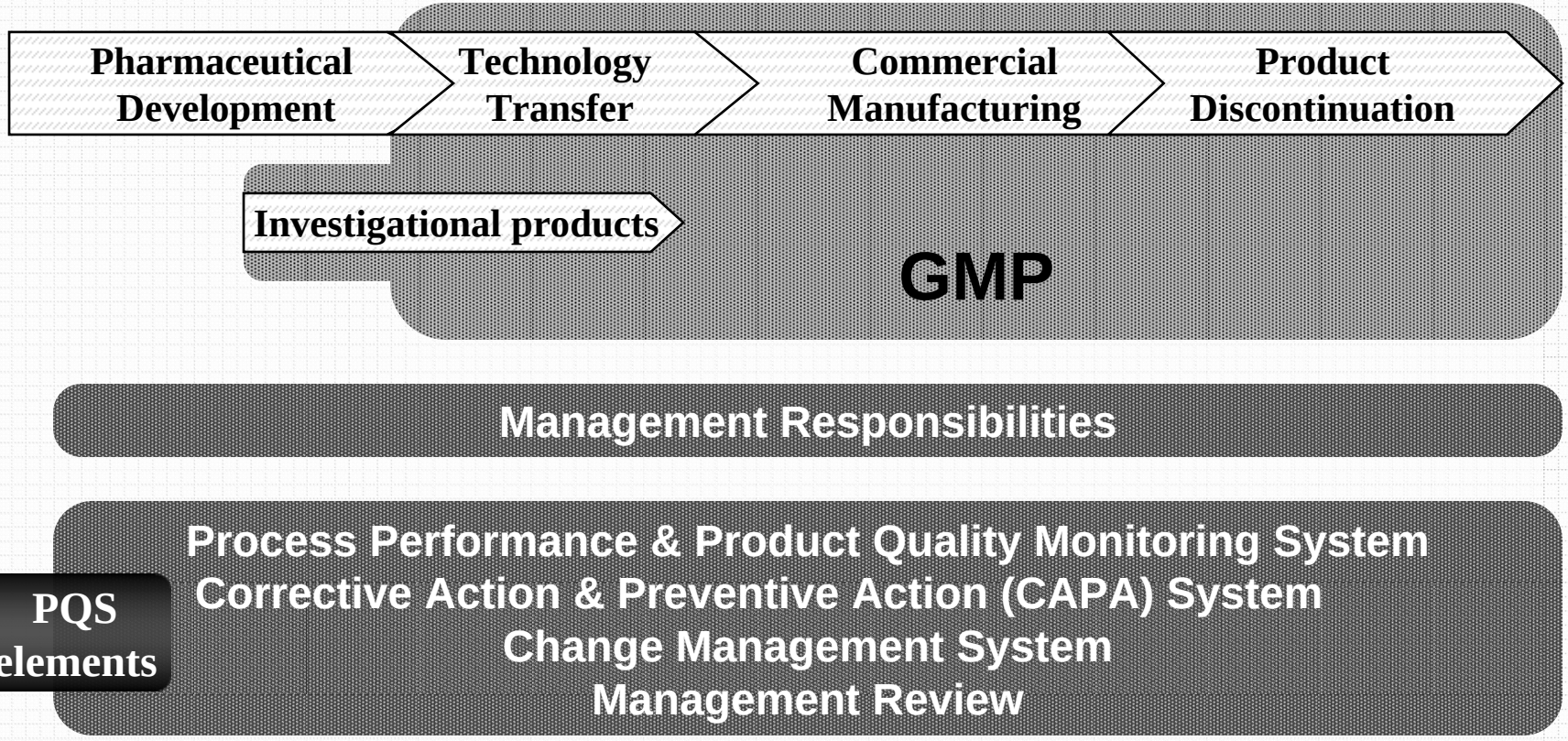
The next horizontal bar in the diagram illustrates the importance of management responsibilities explained in Section 2 of the diagram to all phases of the product lifecycle

ICH Q10 Pharmaceutical Quality System



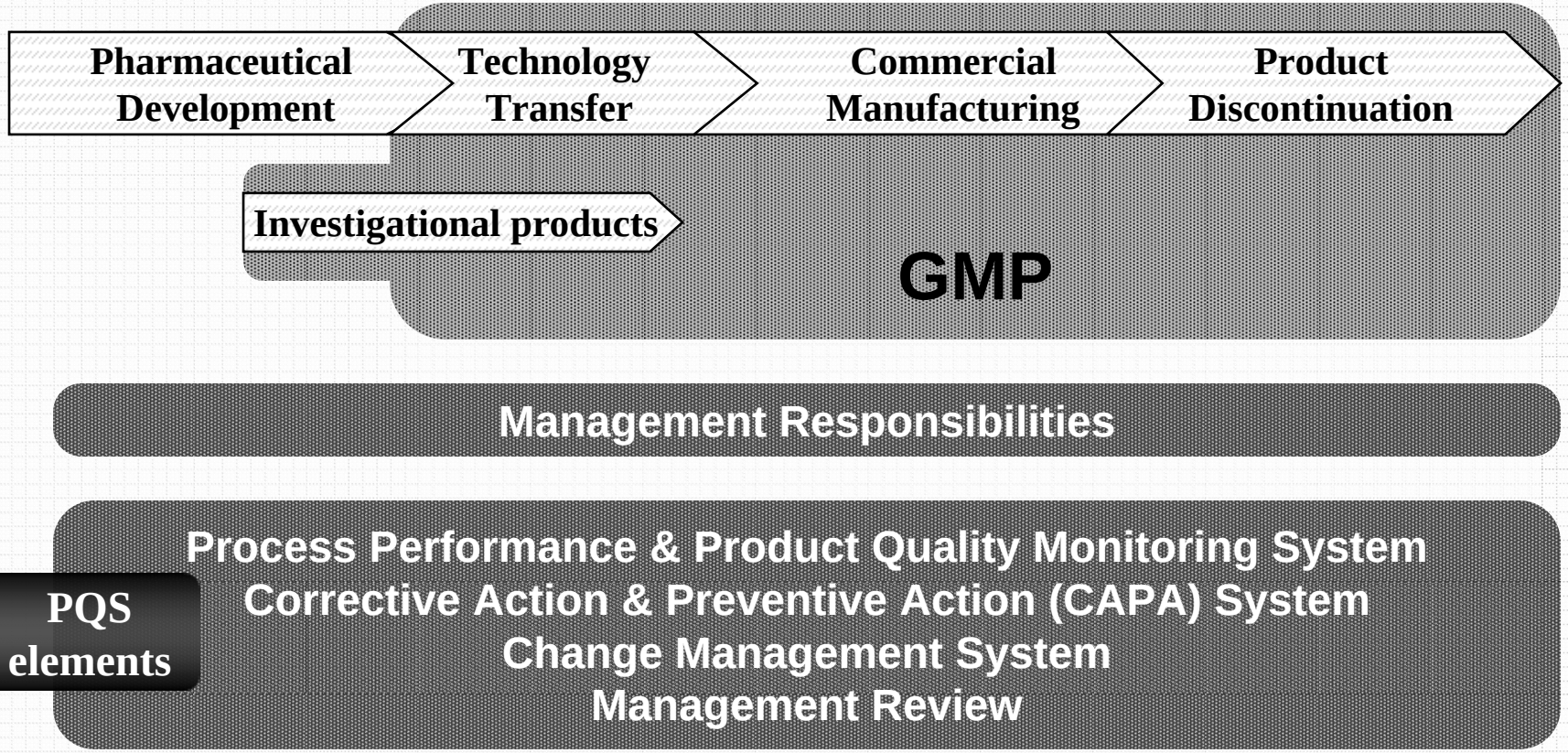
The diagram in the next lower section lists the PQS elements which serve as the major pillars under the PQS model.

ICH Q10 Pharmaceutical Quality System



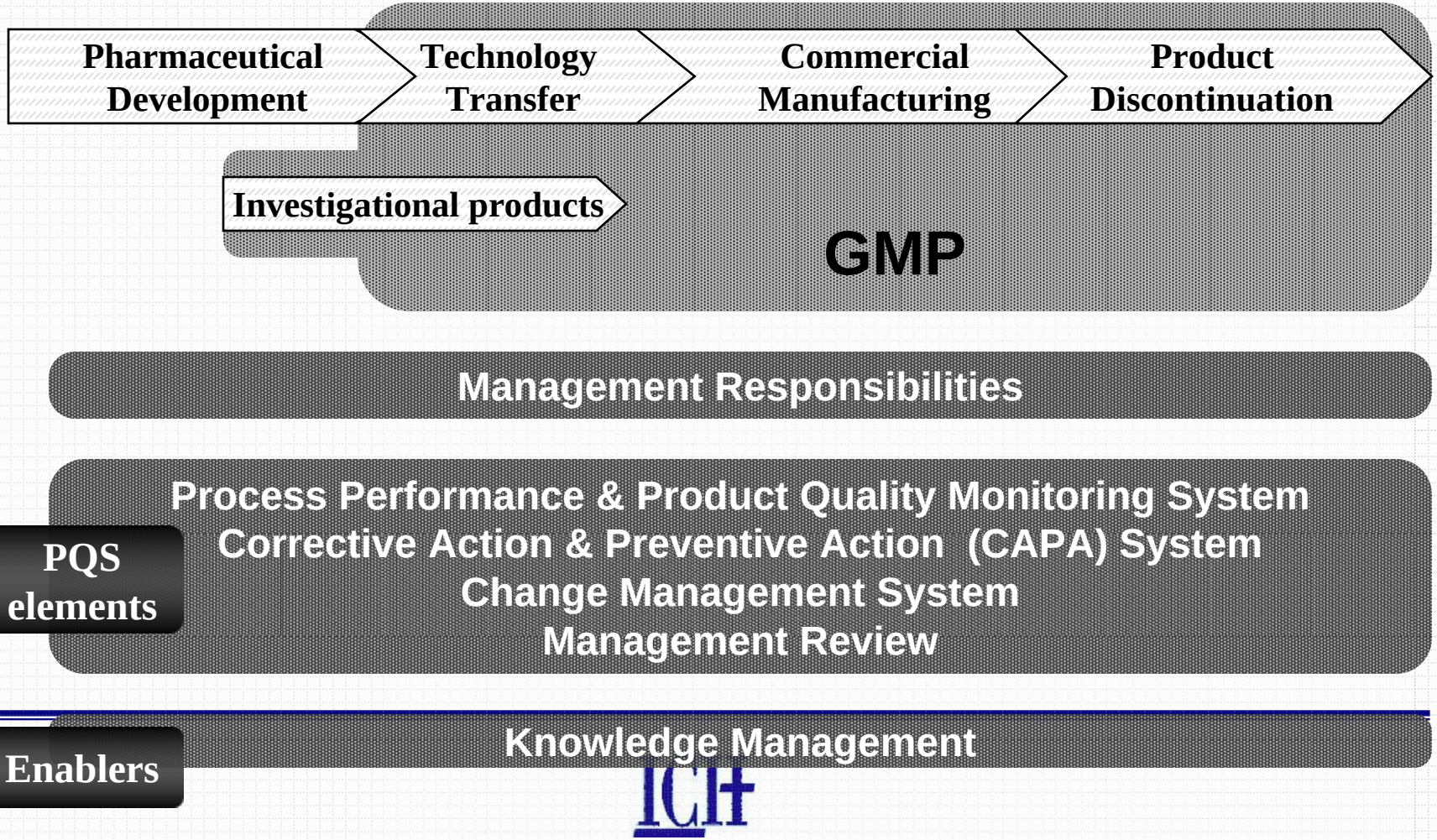
These elements should be applied appropriately and proportionally to each stage recognizing opportunities to identify areas for continual improvement

ICH Q10 Pharmaceutical Quality System



The bottom set of horizontal bars,
illustrates the enablers
which are applicable to all of the lifecycle phases

ICH Q10 Pharmaceutical Quality System



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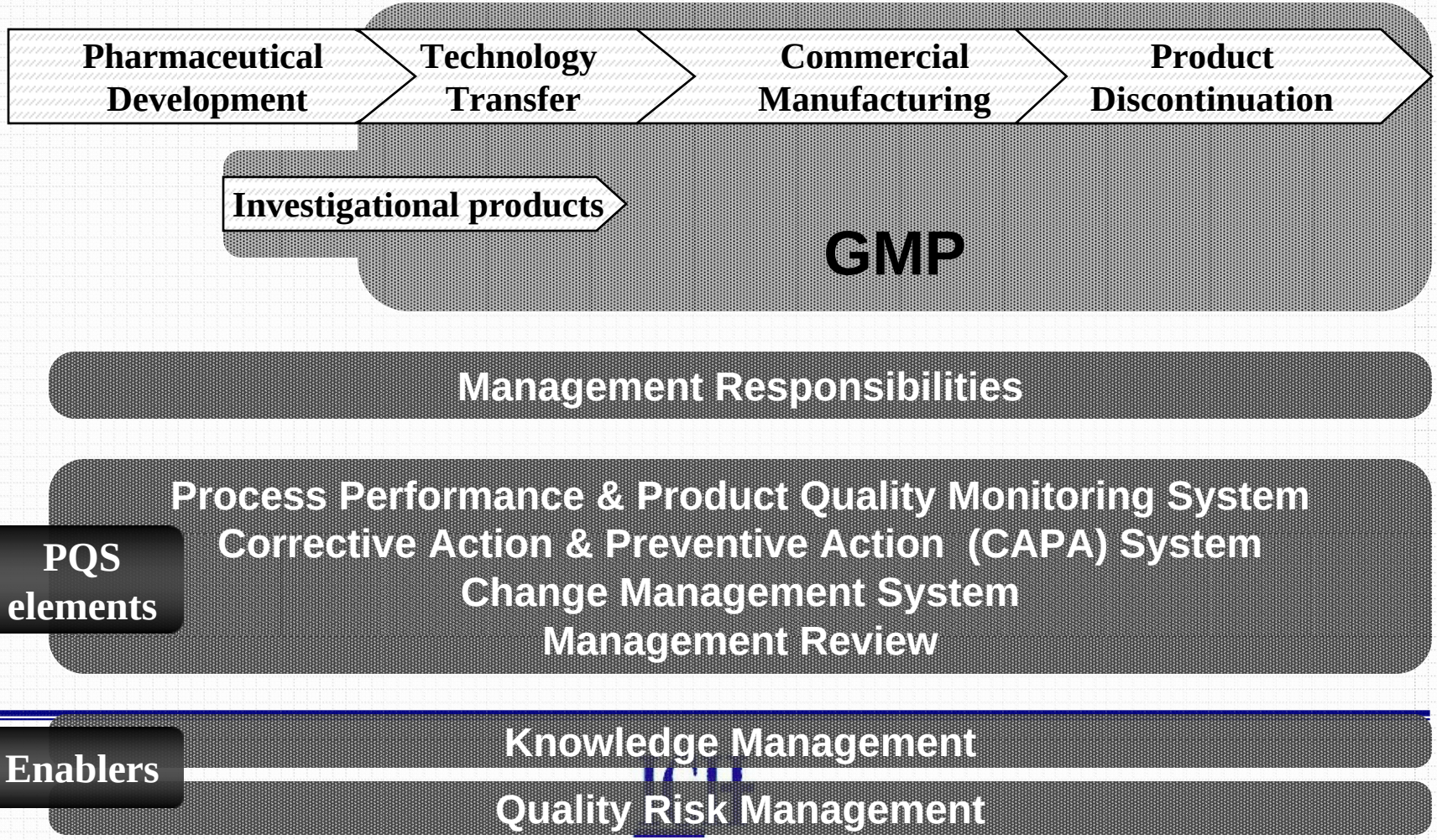
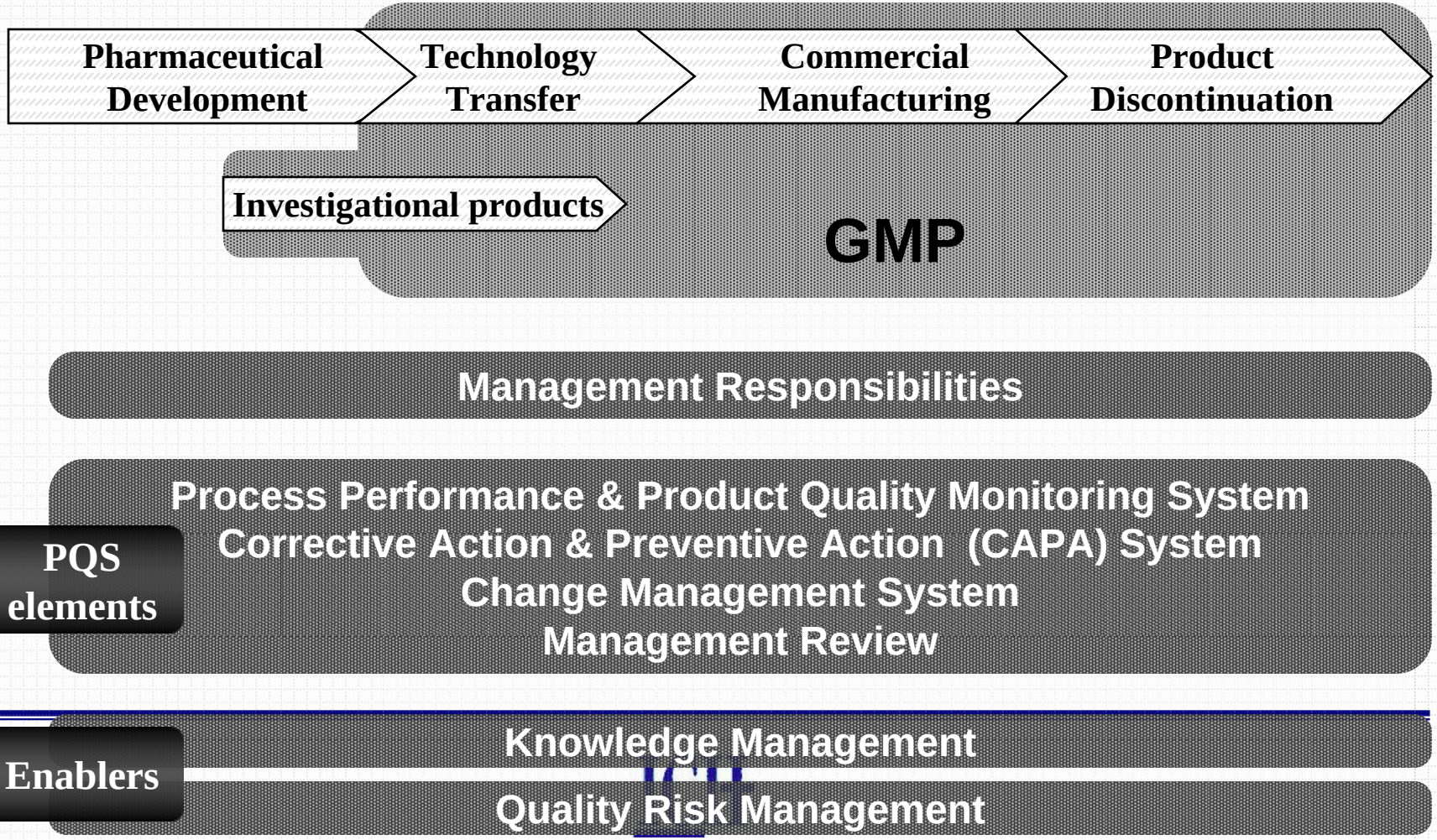
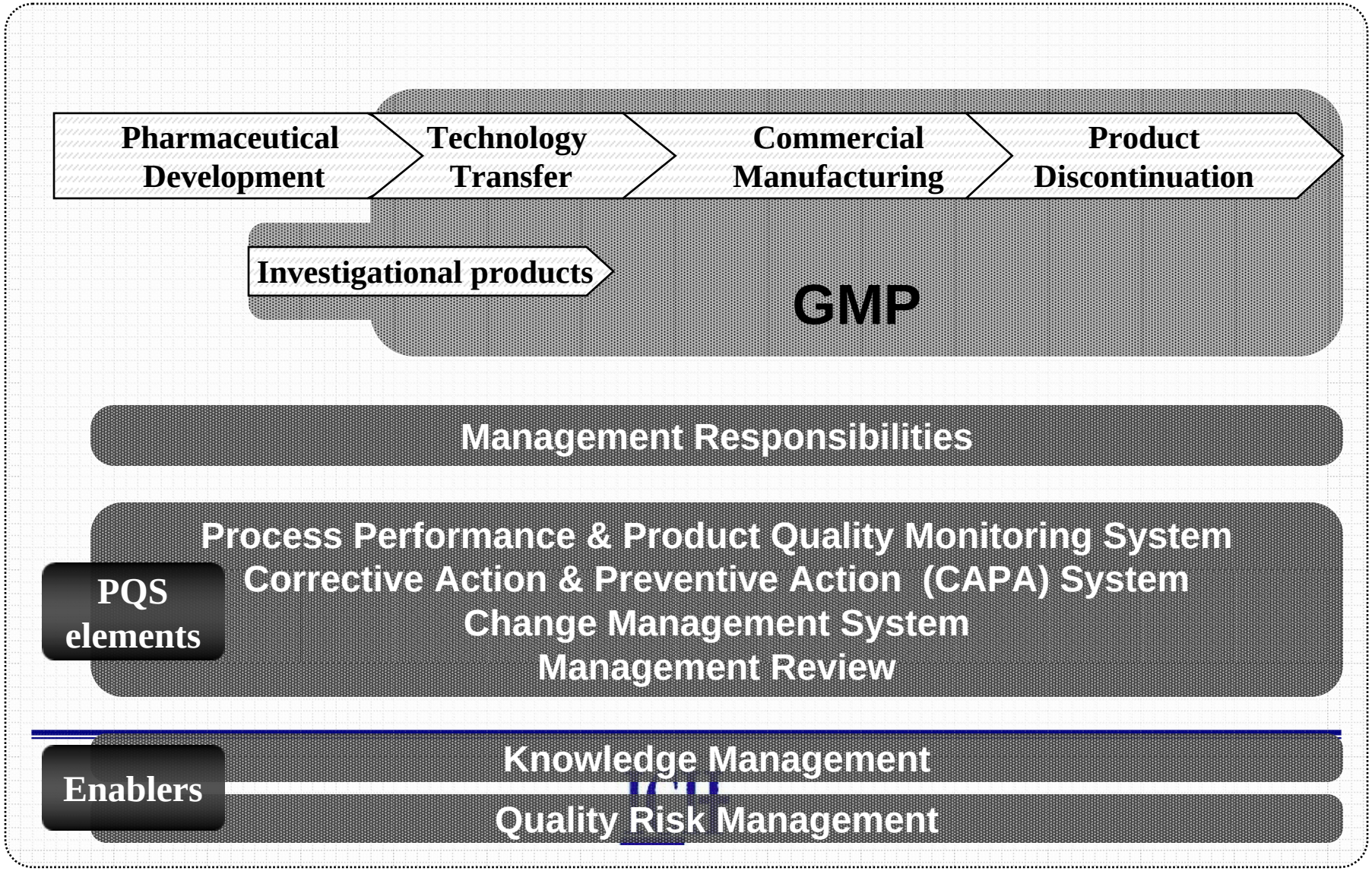


The Enablers support the PQS goals of achieving product realisation, establishing and maintaining a state of control, and facilitating continual improvement

ICH Q10 Pharmaceutical Quality System



ICH Q10 Pharmaceutical Quality System



EFPIA/ PAT seminar course in Ireland - April 08

- Initiative between EFPIA & EMEA PAT Group
- Site visits was recognised as extremely useful to both industry and regulators
- Two site visits were involved observing the real life application of the principles of Quality by Design (QbD), Design Space (DS) & PAT (Process Analytical Technologies)
- The meeting in Ireland provided a forum to openly discuss the outcome of the visits and identify those priority action items to be followed up
- The main discussion points arising from each of the site visits are presented in the following slides

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Mock Inspections

- Development Site Inspection
  - not to become routine (dependant upon complexity of the application etc). GMP not a requirement at a development site
  - Discussion in respect of the amount and type of development information that would need to be available during an inspection
  - Role of inspector & assessor
- Manufacturing Site Inspection
  - Better understanding of knowledge transfer from development to manufacturing
  - Translation of the DS into the routine manufacturing environment

Feedback from Regulators

- QbD does not automatically mean there will be DS or Real Time Release (RTR)
- Understanding of what a Design Space actually is varies (the multivariate interactions between parameters and product attributes)
- Some confusion around the following:
  - Proven Acceptable Ranges (PAR)
  - The terms 'Control Strategy' and 'PAT'
- Overall it was felt that there is a need to communicate the risk strategy to the regulators

Conclusions

- Very useful event in gaining an understanding of current thinking by regulators and industry
- Use of real-life examples was particularly beneficial
- A range of issues that require further discussion and reflection have now been identified (Criticality…)
- Many common issues were identified, some between regulators, some between industry and some between industry and regulators

- Very Good input for IWG

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Agenda Brussels meeting

1. Adoption of the agenda
2. Objectives/expectations of Brussels meeting
3. What can be achieved:
   a. short term
   b. medium/long term
4. Discussion on different topics, elaboration of Q&A:
   a. Knowledge Management (MHLW/JPMA)
   b. QbD topics (FDA/PhRMA)
   c. PQS: (EU/EFPIA)
5. Training issues: workshops, set of shared (agreed) slides,…..
6. Collaboration with other organisations: setting up of a procedure
7. AOB

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Brussels meeting's Topics for Q&A

	Quest. Agreed	Total Quest.	Lg Term Topics
Quality by Design (QbD) topics	1	1	-
- Design space	7	7	1
- Real Time Release Testing	9	10	1
- Control Strategy	3	4	0
- Criticality	-	-	1
Pharmaceutical Quality System	12	12	1
Knowledge Management	1	5	1
	33	41	5

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Q&A for publications : target

- Internal Review by the 6 Parties / Observers / Interested parties

- Agreed Q&A for publication (March/April 09) before Yokohama (June 09)
- Collect additional questions through the ICH Secretariat (IFPMA)
  - Cluster / Filter the questions
  - Review during Yokohama

Examples of Questions (Still Draft)

- **Knowledge Management**
  - How has the implementation of Q8, Q9 & Q10 changed the significance and use of Knowledge management
- **Pharmaceutical Quality Systems / Inspection**
  - How does a company demonstrate implementation of PQS in accordance with ICH Q10 ?
  - What information and documentation of the development studies should be available at a manufacturing site ?
  - Will there be a ICH Q10 certification ?
- **Quality by Design**
  - Does a set of proven acceptable ranges alone constitute a design space ?
  - Is it possible to develop a design space for existing products?
  - Is a product specification still necessary in the case of RTR testing

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Q&A for further considerations

- **Referring to relevant case studies, examples, detailed documents and further discussions e.g.**
  - **Design Space for multiple unit operations, scale up and site change**
  - **Statistical considerations for sampling and acceptance criteria for Real time release testing**

Other Aspects

- Training issues
  - Common training package
  - In and outside ICH region - ?
- Collaborations with external parties and organisations

Training

- Objective
  - Make sure that the correct and consistent interpretation is presented
- Common training package
  - Setting up a common set of agreed slides
    - (As a ICH Q9 model briefing pack)
- Workshops
  - Co-sponsorship by Q-IWG
- External Technical input
  - Not-for-profit organisations with a global reach
  - Only technical and scientific contribution will be considered
  - Q-IWG endorsement

Next steps to Yokohama

- Review initial Q&A by regions
- Intermediary work
- Publish initial Q&A after endorsement by ICH-SC
- Identify additional topics for Q&A

Future Expectations

A big challenge for regulators and industry

- **Trust** : How confidence between regulators and industry is beginning to grow,
- **Common understanding** :The interest to better define concepts already existing but without common understanding and way to use
- **From Theory to Practice** :The shared will to work together from virtual, concepts to practical implementation till the end of the process
- The strong wish to ***facilitate innovation*** and envisage ***"regulatory flexibility"*** within the common interest of ***protecting patients and public health***.

Q8,Q9 & Q10 environment : More paper ?

Thank you

NO ! But Harmonised Quality System, based on QRM and Good Science