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Session III : Track IIb

Drug Product Manufacturing and Control

Method Development in a QbD Environment

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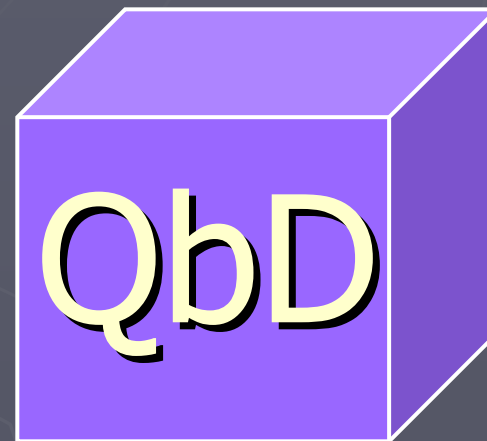
Quality cannot be tested into products
Quality should be built in by *Design*.

A Tool for Regulators

Flexible Regulatory Approach

Design Space

PAT



ICH-Q8

ICH-Q9

ICH-Q10

Scientific Thinking

Risk Evaluation

Life Cycle Approach


Risk Management

Just a Jargon !

What is QbD ?

- ▶ QbD : Quality by Design
- ▶ A systematic approach to development (Q8R1)
- ▶ begins with predefined objectives (QTPP)
- ▶ emphasizes product and process understanding and process control (Design space)
- ▶ based on sound science and quality risk management (Q9)
- ▶ A paradigm shift and not a Jargon !!

QbD : A Paradigm shift

Traditional		QbD
Regulation		Flexible Regulation
Guidance		Flexible Guidance
Development		Efficient Development
Risk evaluation minimal		Well controlled processes
GMP / Quality System		Control over change

ICH-Q8

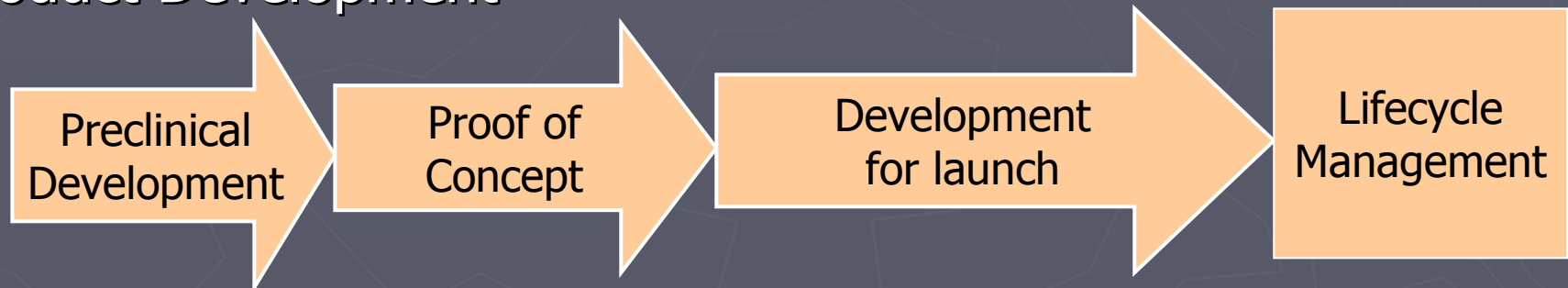
- ▶ ICH-Q8(R1) guidance of Nov.2008 is at Step-4
- ▶ In the core guidance of Q8, QbD was more concentrated on product development and manufacturing process development
- ▶ At that time, QbD remotely implied to analytical methods
- ▶ QbD can now be extended to method development
- ▶ Annex clarifies key concepts with illustrated examples, including method development QbD

Design Space

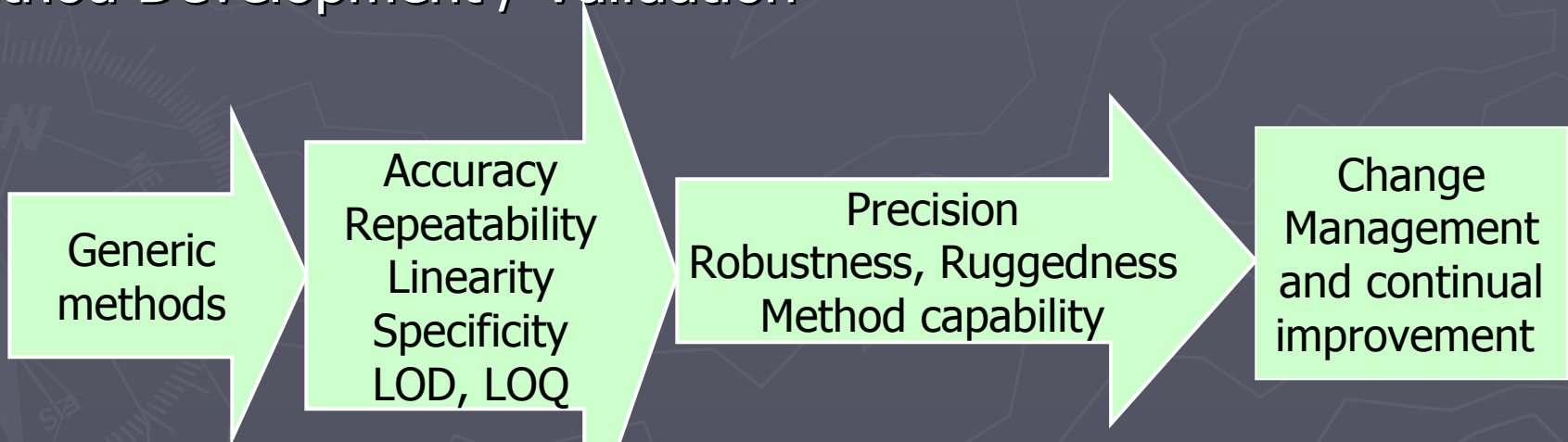
- ▶ The multidimensional combination and interaction of input variables (e.g. material attributes) and process parameters that have been demonstrated to provide assurance of Quality.
- ▶ DS is proposed by the applicant and is subject to regulatory assessment and approval.
- ▶ Working within the DS is not considered as a change

Linkage : Process Vs Method development

Product Development



Method Development / Validation



A few cases ...

1. Process control for an active substance with multiple chiral centers
2. Detection and control of potential genotoxic impurities
3. Failure in Bioequivalence studies
4. Controlling Biotechnological processes
5. How to establish similarity of Biopharmaceuticals and their generic versions ?
6. Is the quality and efficacy of every batch produced, similar to the batch(es) used in clinical trials ?
7. Heparin case : How to avoid recurrence ?

A few analytical cases...

1. How to reduce the variability in dissolution testing?
2. To what extent can a monograph method be changed?
3. Am I allowed to change the detection wavelength mentioned in monograph?
4. Can I substitute the mobile phase mentioned in the monograph? e.g. CH₃CN, ethanol.
5. GC-Headspace dual column method for Residual solvent analysis - Split ratio, column and speed.

Questions are not new,
but method development in a QbD environment
can provide enhanced and effective outcome

Acknowledgements



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