Quality by Design (QbD) for Pre-Filled Syringes (PFS)

Paul Seminara CEng MBA

Balcary Ltd

What?

- A systematic approach to development that begins with predefined objectives and emphasises product and process understanding and process control based on sound science and quality risk management. [ICH Q8]

Why?

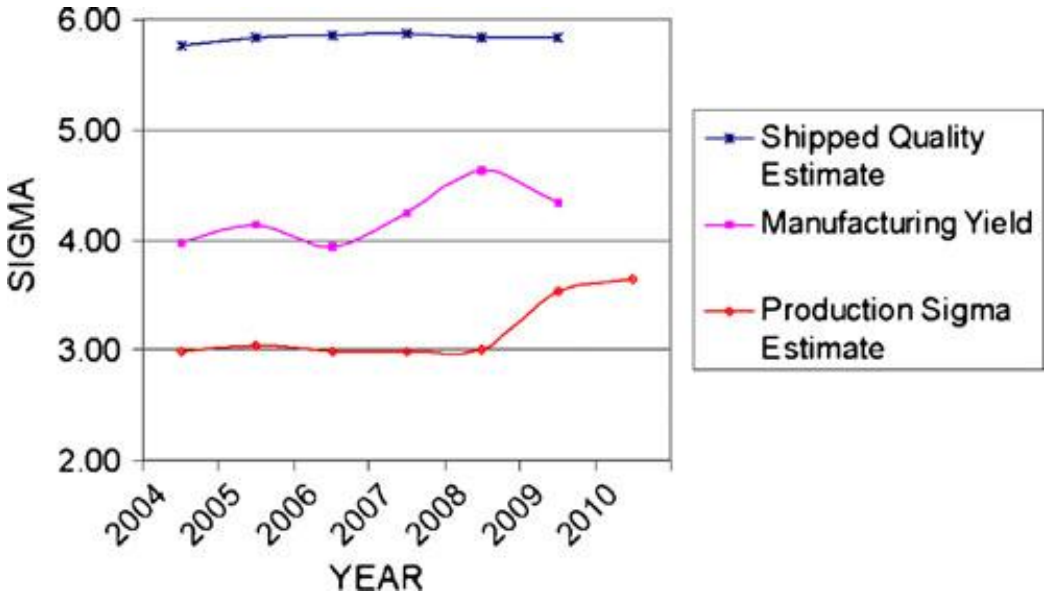
- Protect the patient.

- Ensure that marketed batches have the same safety & efficacy profiles. Risk to the patient is minimised by decreasing variability.

- Goal : process that is insensitive to disturbances. Robust.

Cost

Quality sigma trends

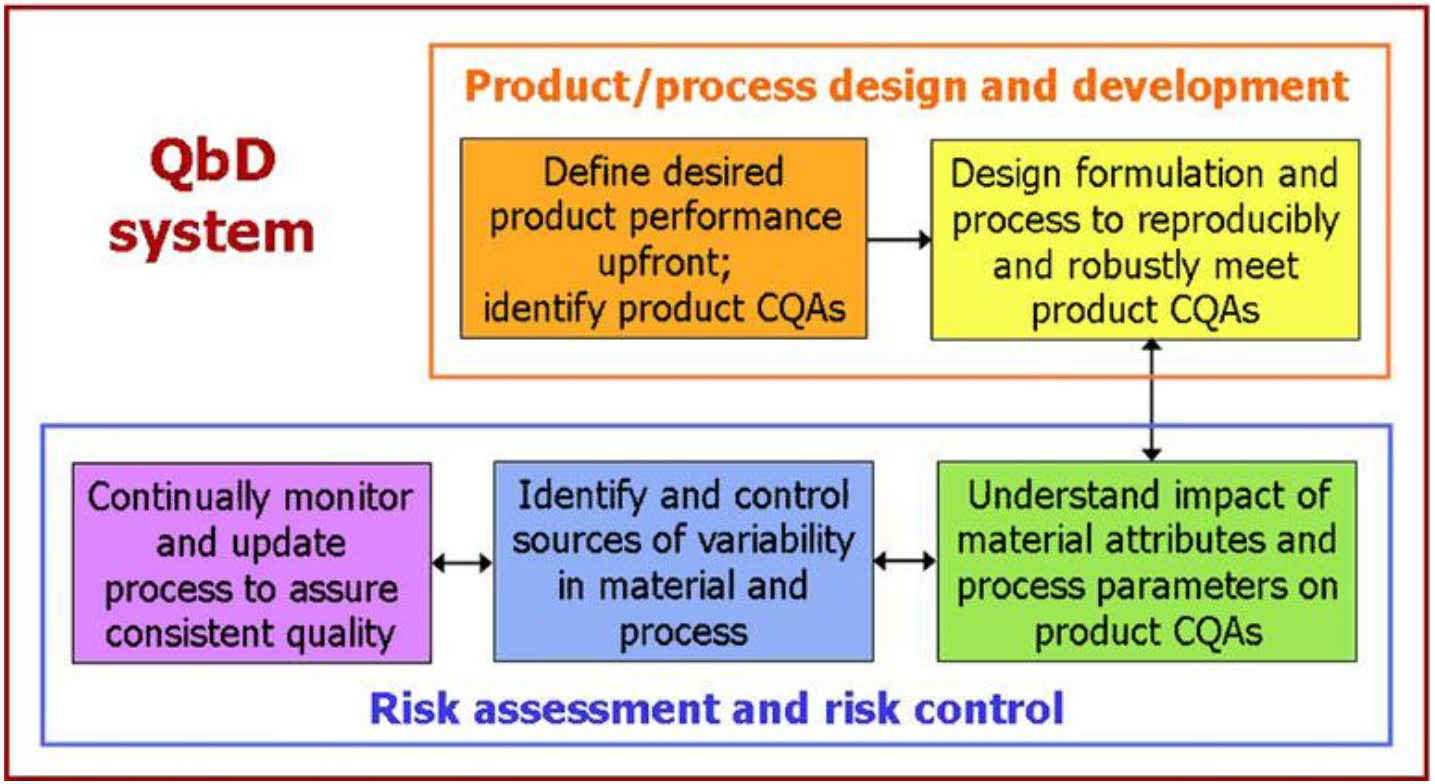


"Ultimate success (for industry and regulators) is having affordable drugs for the patient."

"Industry, academia and FDA must work together to find ... less costly ways to turn good biomedical ideas into safe and effective treatments."

Overcoming Inherent Limits to Pharmaceutical Manufacturing Quality Performance with QbD
Timothy D. Blackburn & Thomas A. Mazzuchi & Shahram Sarkani

FDA View on QbD

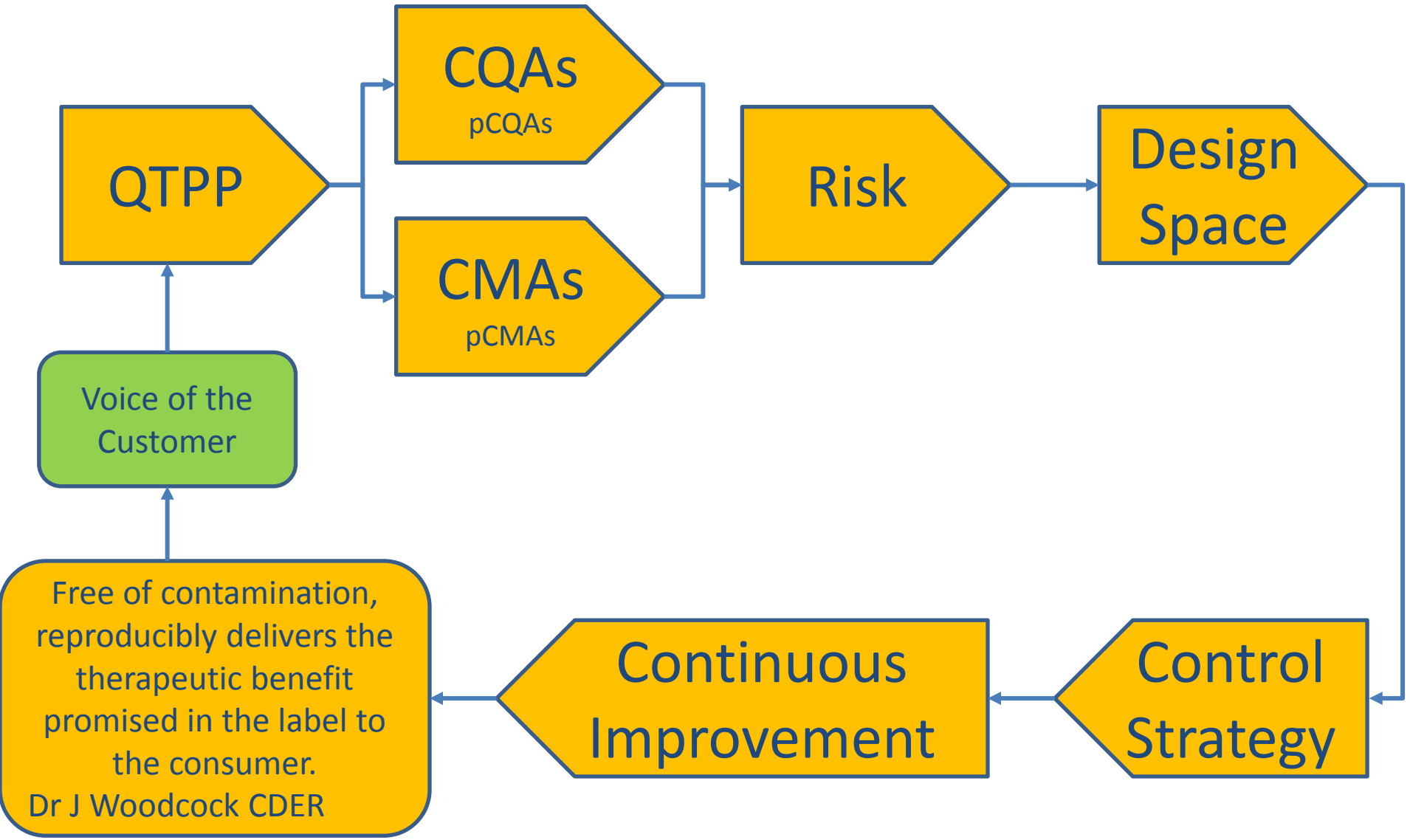


- Sterile products are minority dosage forms.
- Manufacturing process is extremely critical.
- Utilisation of PAT and QbD for sterile products so far is still limited.

The Agency strongly encourages the use of the QbD concept, but stability testing would continue to be part of a regulatory submission.

Regulatory Perspectives on Product Stability
Gary Buehler and K. Huynh-Ba, 2010

QbD Implementation



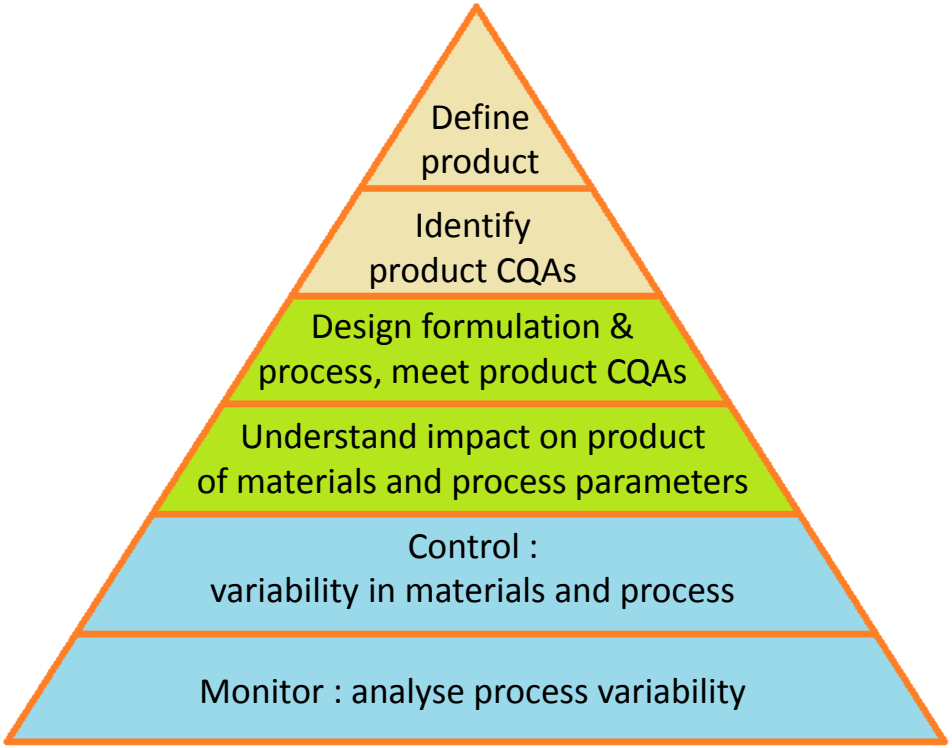
QbD

QTTP	CQAs CMAs	Risk	Design space	Control strategy	Continuous improvement
• Dose form, delivery system. • Strength. • Container closure. • Sterility, purity.	• Potential CQAs. • Purity, particle size, sterility, bulk density, viscosity, .	• Prioritise. • FMEA.	• CPP. Map ... • Material and process variables. to ... • CQAs • Design of Experiments. • Multivariate.	• In-Process Controls. • Product specifications • Sterilisation parameters. • Bio-burden control. • PAT	• Reduce variation to target values. not... • Response to CAPA.

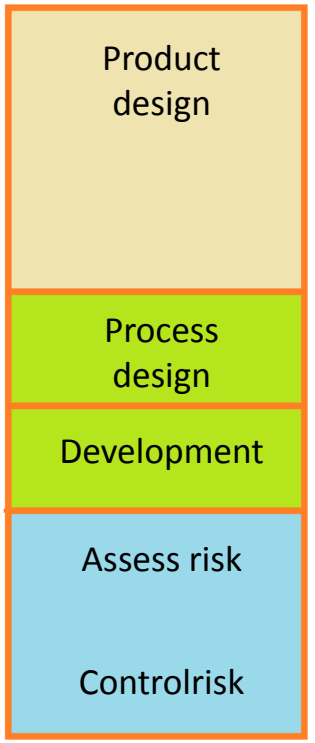
Required
- Quality Target Product Profile
- Product understanding
- Process understanding
- Control strategy & justification

Optional
- Design space
- Process Analytical Technology

QbD System

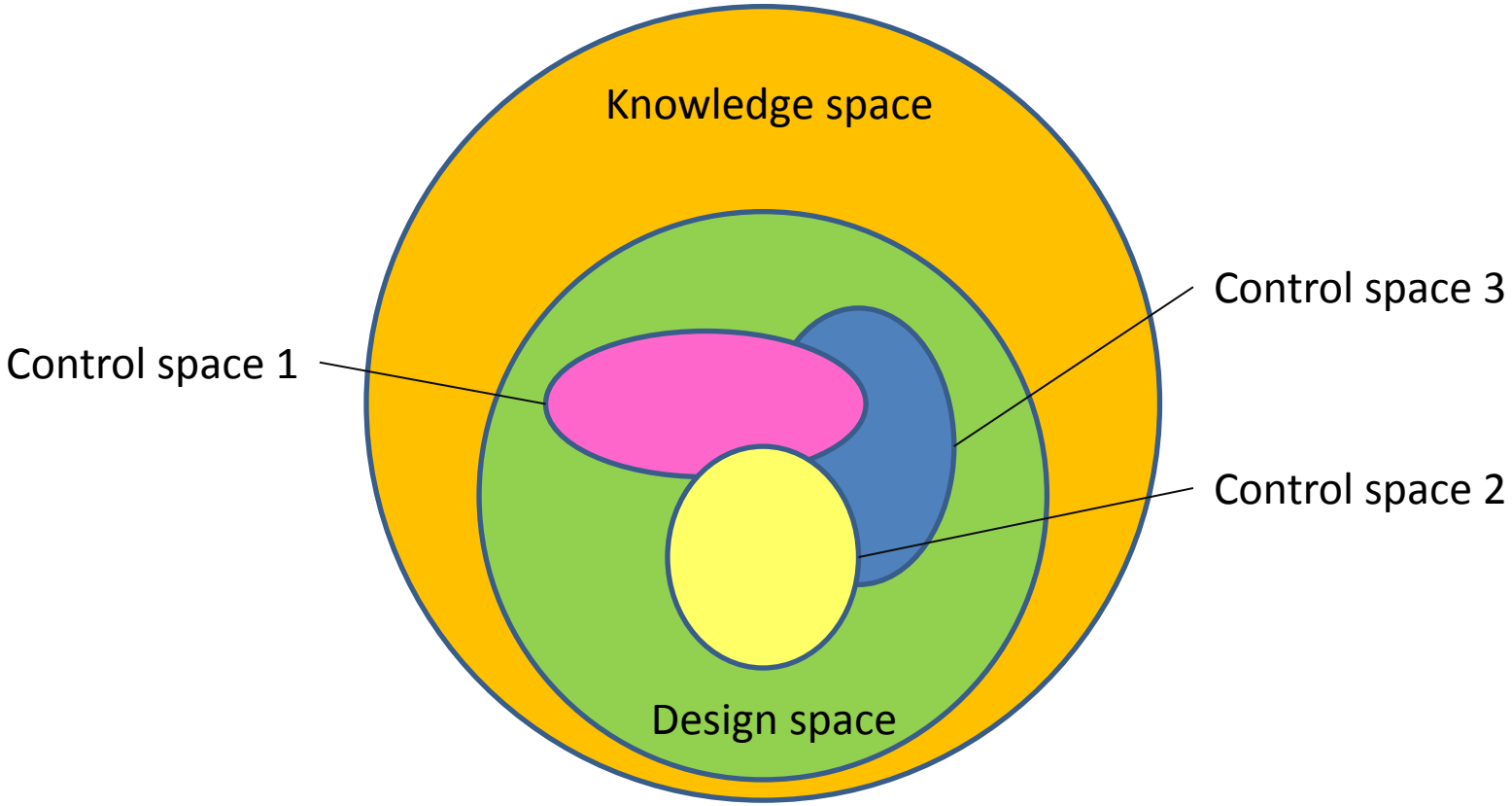


Critical Quality Attribute CQA



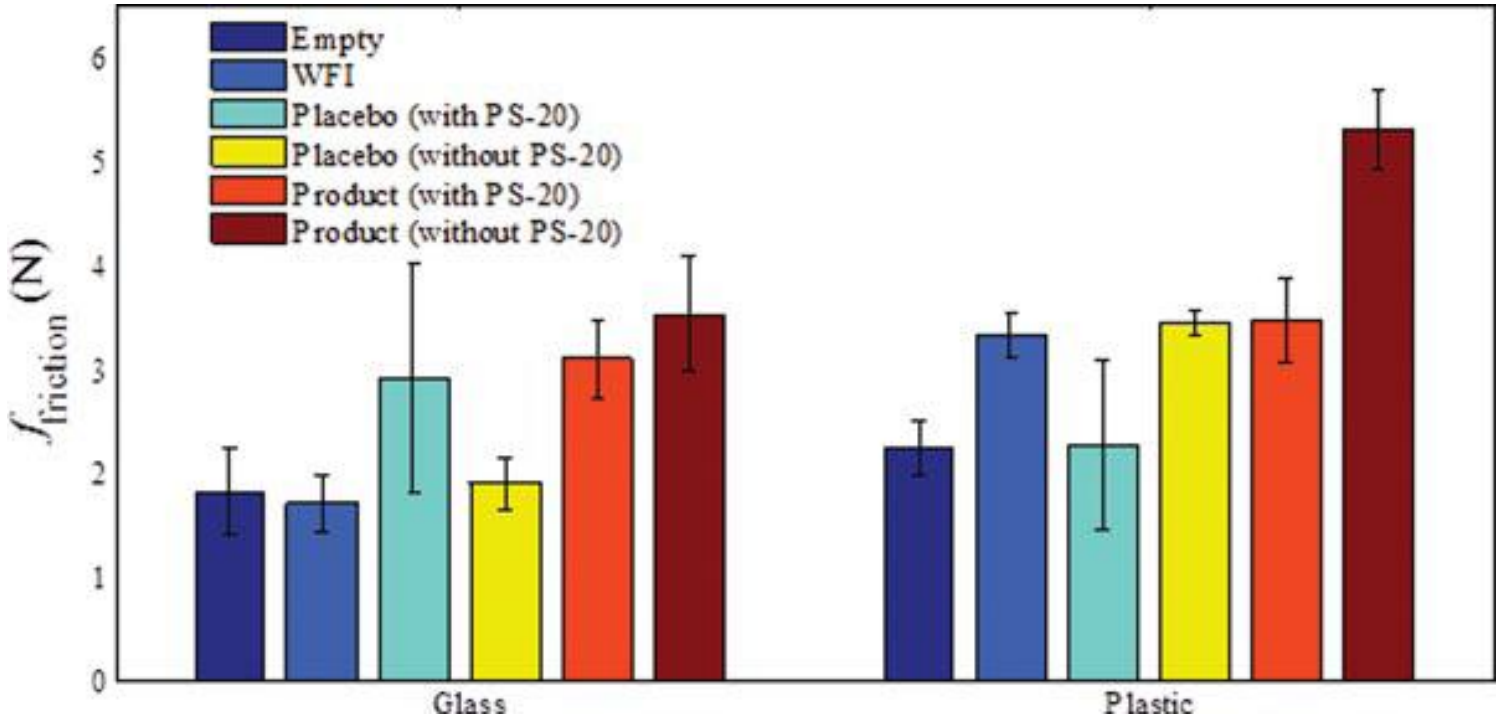
The Concept of Quality-by-Design
Mark A. Staples

Design Space



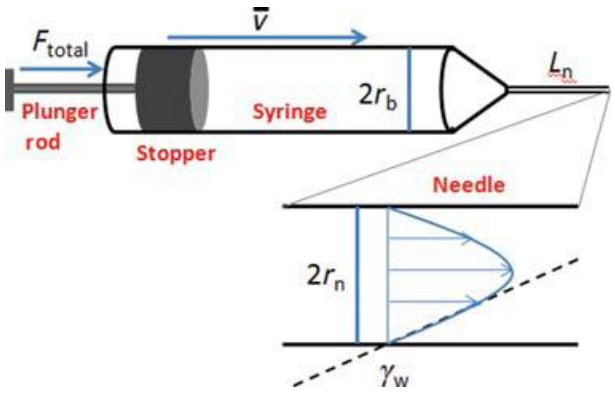
The range of possibilities within which process parameters may be varied without compromising product quality over the shelf life of the product.

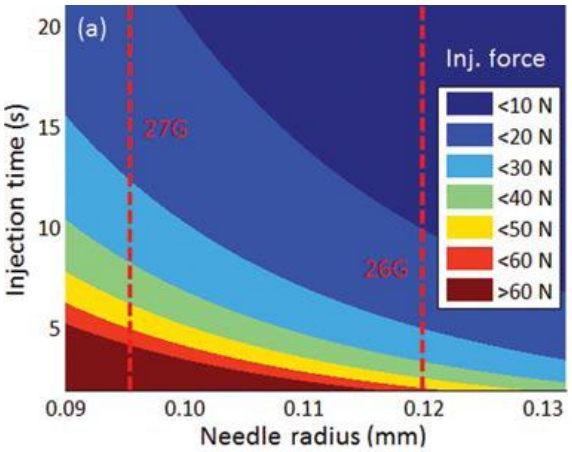
Design Space

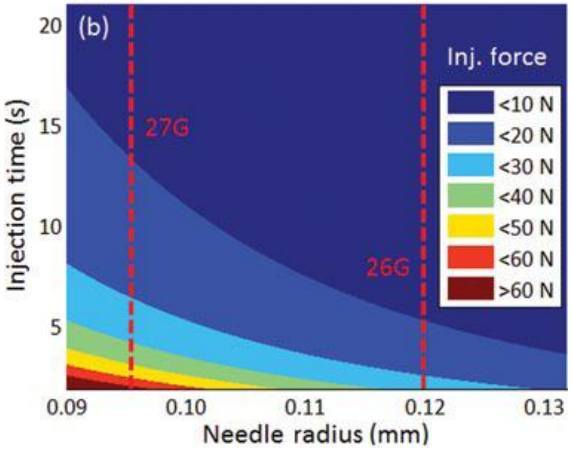


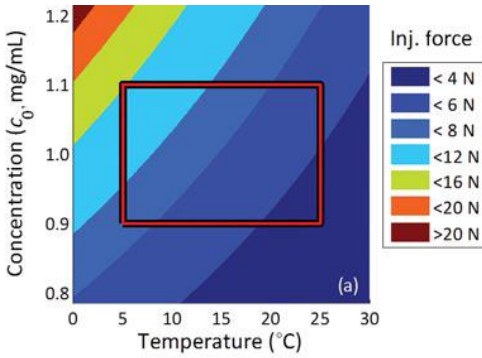
Product–Syringe Interaction and Its Impact on $f_{friction}$

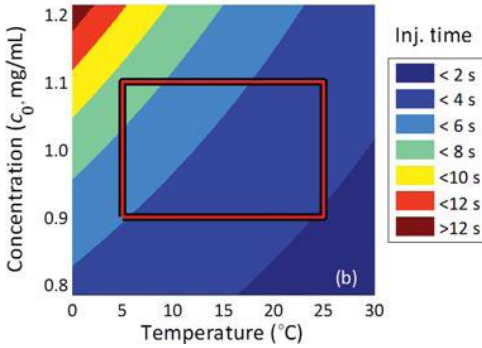
Design Space











Effects of shear thinning

a. Newtonian
b. non-Newtonian

Effects of temperature

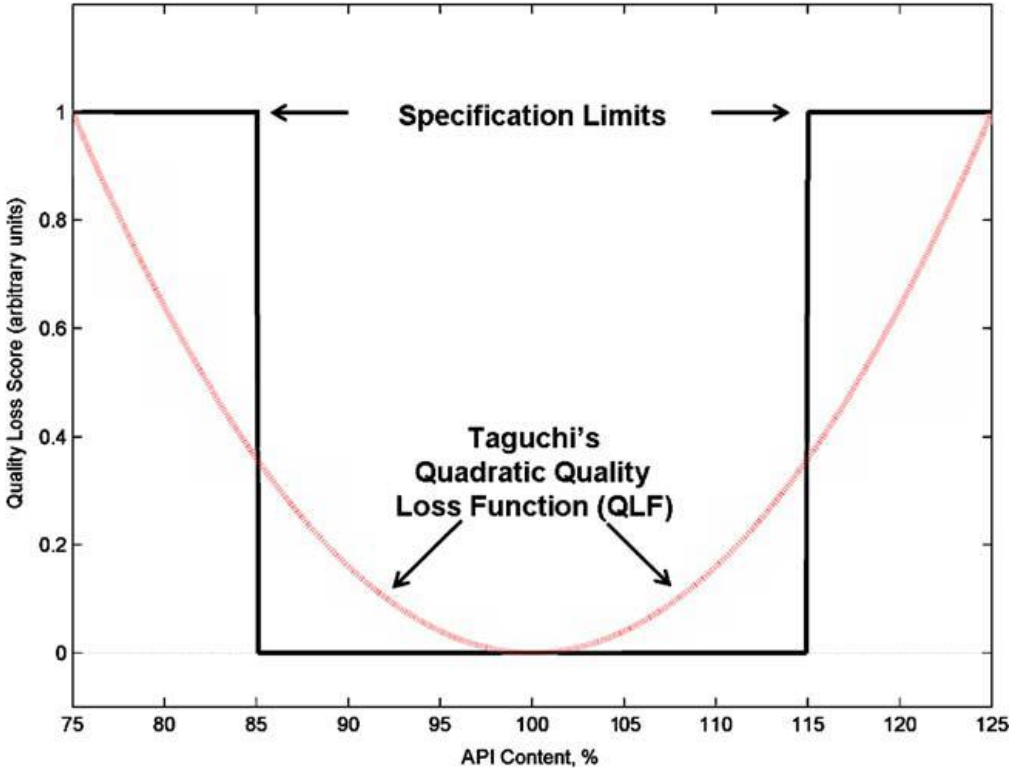
- Storage temperature.
- Operation at low temperature.
- Equilibration time.

Taguchi

Much less attention to TPP

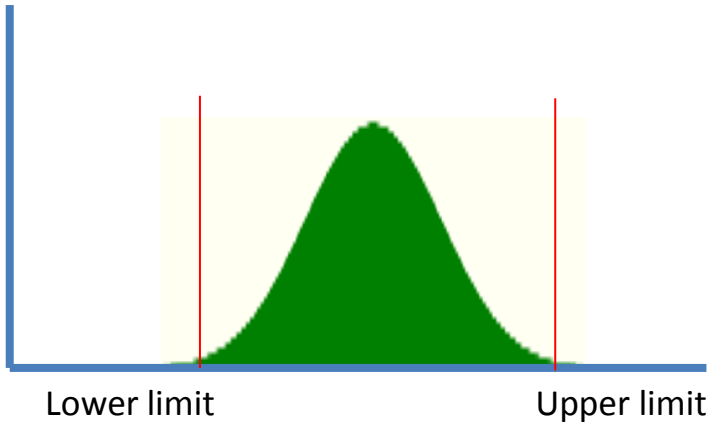
- Target product profile
- Product critical quality attributes (CQAs)
- Raw material attributes and process parameters
- Risk assessment
- Design space
- Control strategy
- Lifecycle management and continuous improvement

"It is just as unethical to add tremendous cost to ensure products are of good quality as it is to ship defective goods."

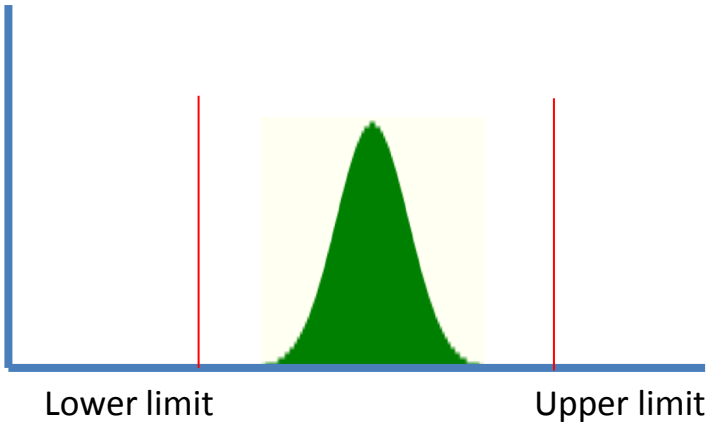


Risk-based Quality by Design (QbD): A Taguchi Perspective on the Assessment of Product Quality, and the Quantitative Linkage of Drug Product Parameters and Clinical Performance
Robert P. Cogdill & James K. Drennen

Process capability



Specification



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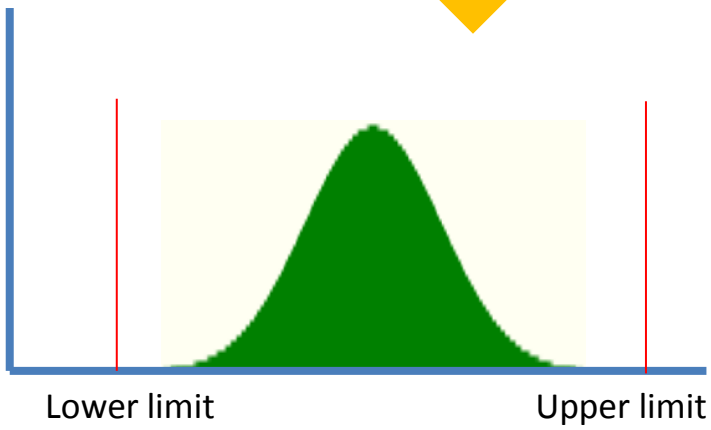
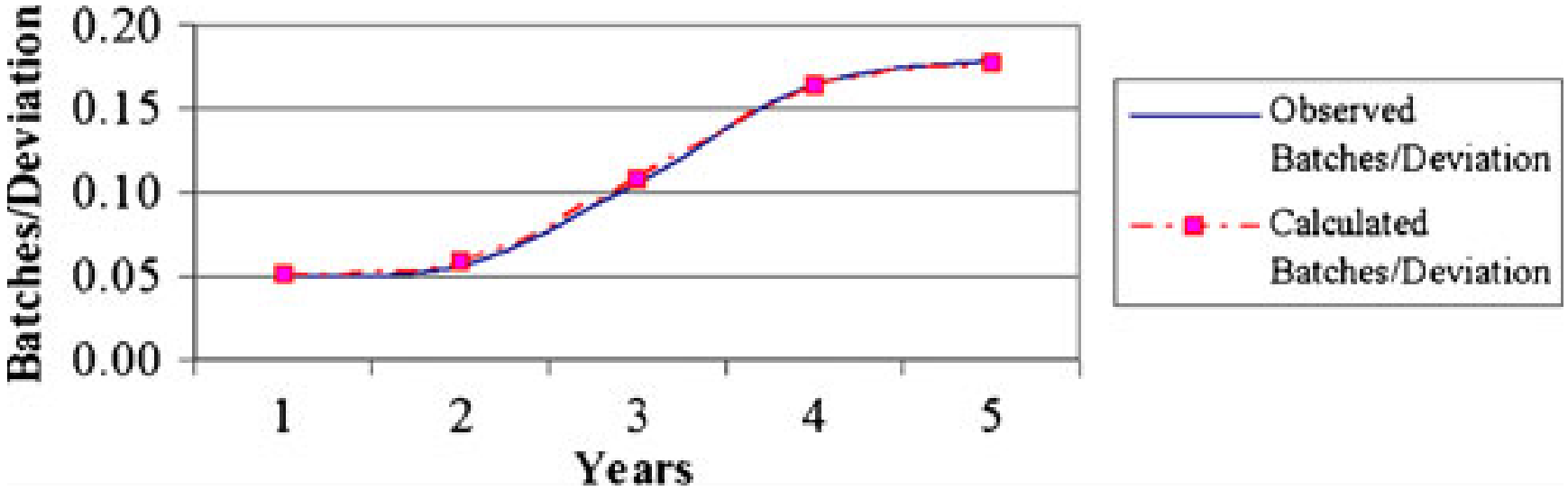


Specification

Continuous improvement



- Reduce variability.
- Tighten specifications.
- Increase process capability.

Reduce variability about nominal
Vs.
Respond to CAPA.

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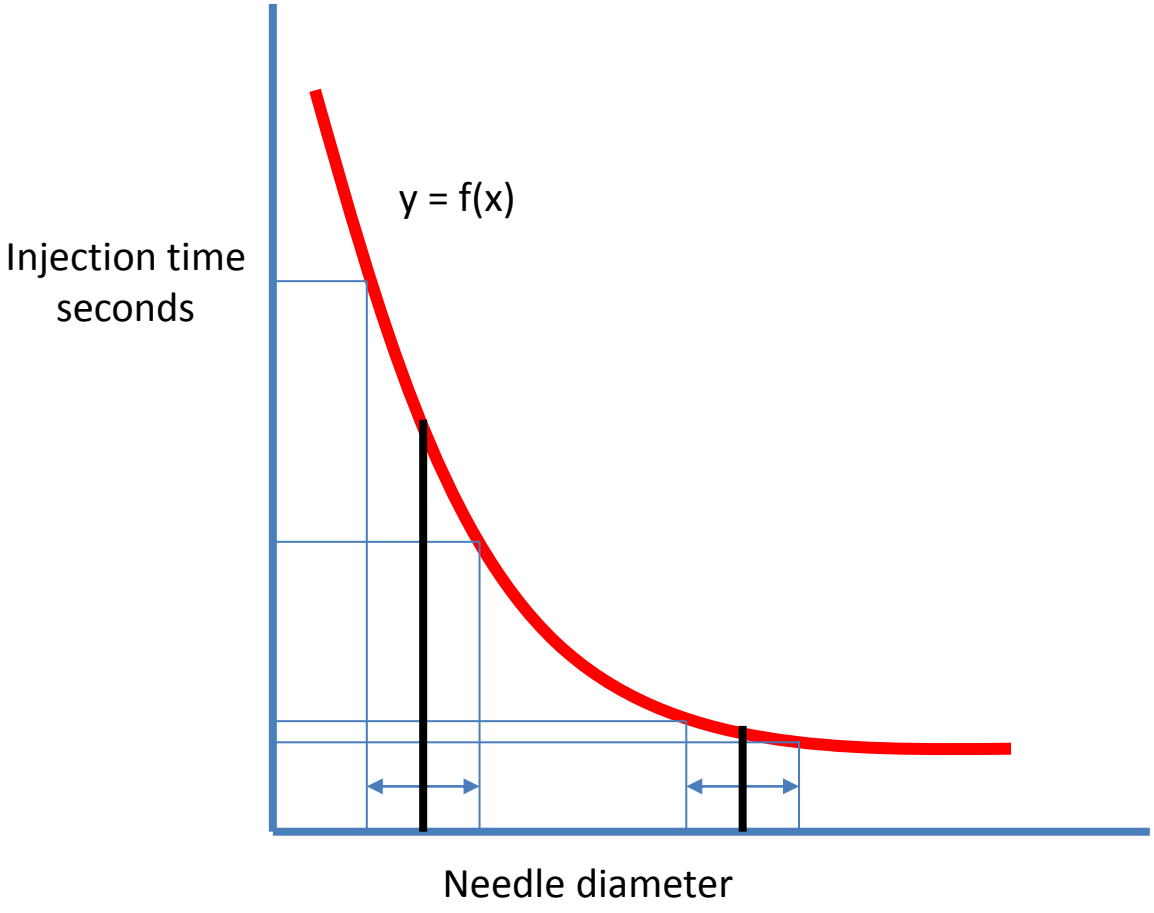
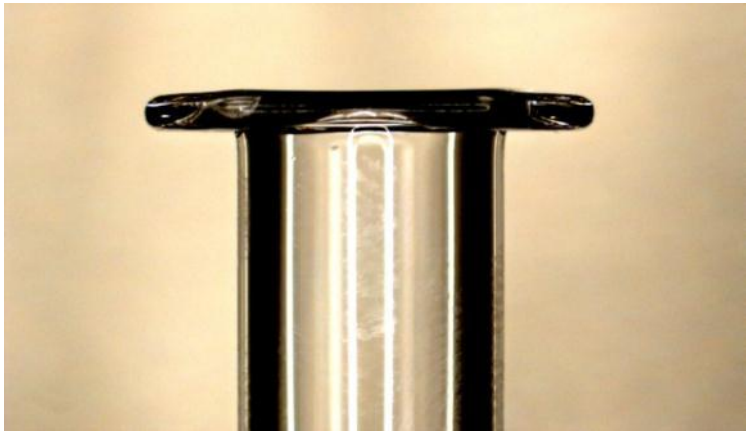
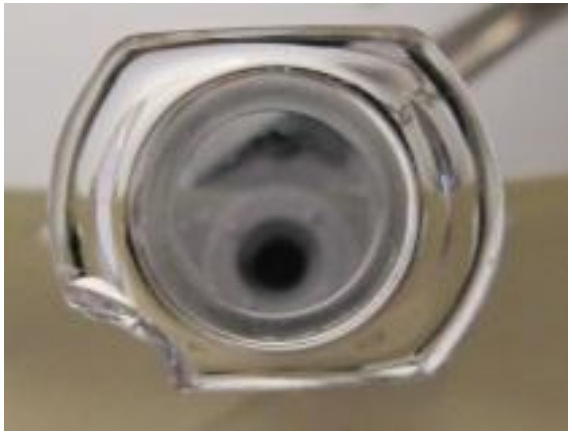
Robust operation

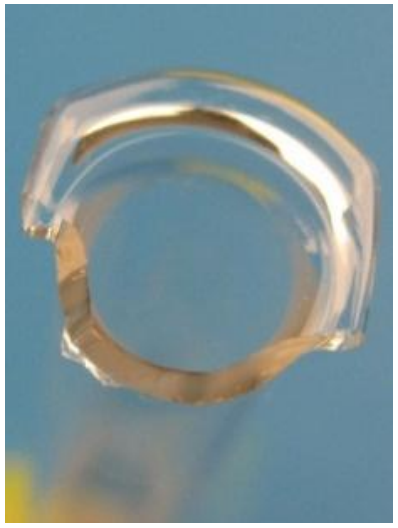


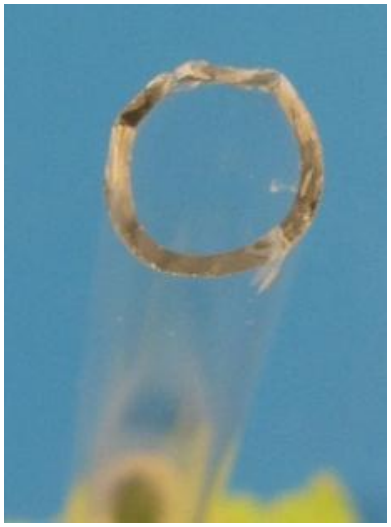
1. Understand the process – the shape of the function.
2. Find operating conditions under which process and product quality are insensitive to normal variations & disturbances.
3. Set specifications on materials and upstream processes to limit disturbances.
4. Use data – DoE.

Design robustness



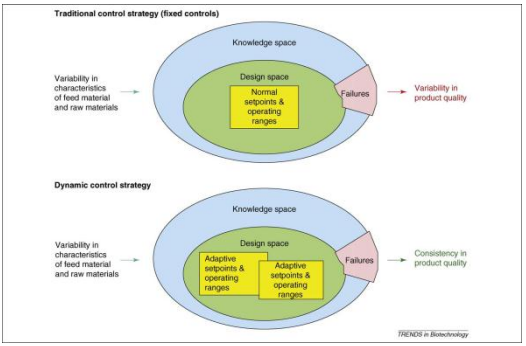


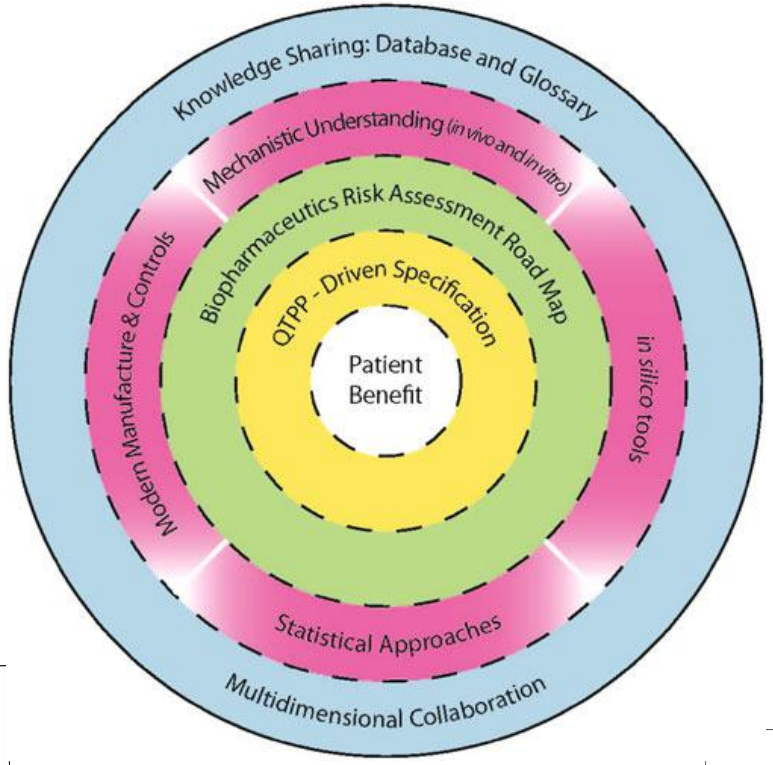




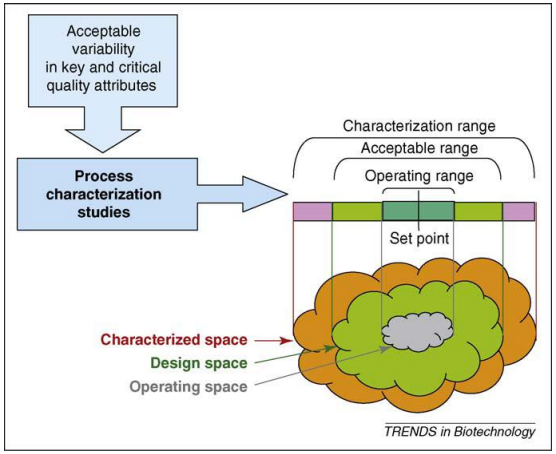
Quality by Design

Control strategy

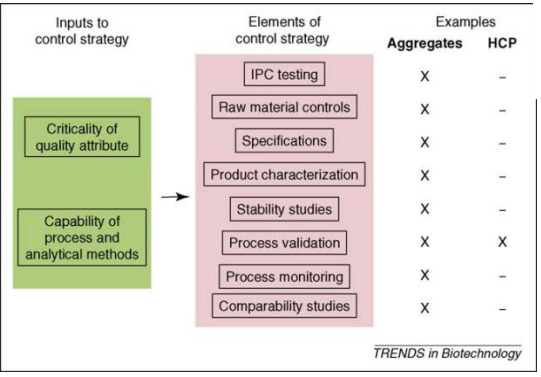




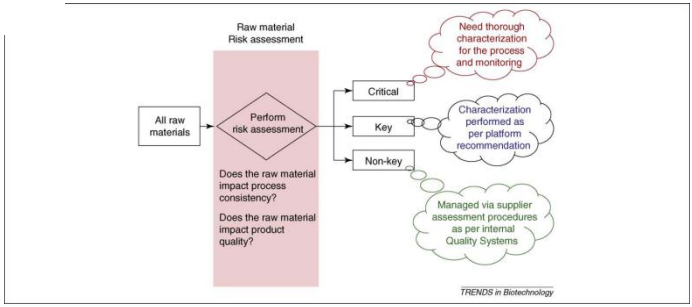
Design space



CQAs, CMAs



Risk assessment



Roadmap for implementation of quality by design (QbD) for biotechnology products
Anurag S. Rathore

Applied Biopharmaceutics and Quality by Design for Dissolution/Release Specification Setting
Arzu Selen, Maria T. Cruañes, Anette Müllertz, Paul A. Dickinson, Jack A. Cook, James E. Polli, Filippos Kesisoglou, John Crison, Kevin C. Johnson, Gordon T. Muirhead, Timothy Schofield, Yi Tsong

Quality by Design

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