Pharmaceutical Manufacturing – Introductory Remarks

NIPTE Research Conference:

Pharmaceutical Critical Path Manufacturing 2015

May 1, 2015

Christine M. V. Moore, Ph.D.

Acting Director, Office of Process and Facilities

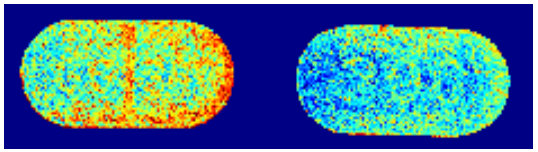
FDA/CDER/OPQ

What is Quality?

The Patient Cannot "See" Quality

Which milk is subpotent?

Which drug is subpotent?



Expectations for Quality

Patients and caregivers assume that their drugs:

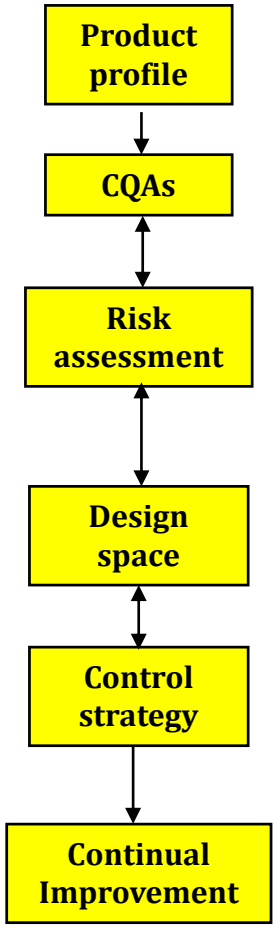
- Are safe, efficacious, and have the correct identity
- Deliver the same performance as described in the label
- Perform consistently over their shelf life
- Are made in a manner that ensures quality
- Will be available when needed

Linking Process - Product - Patient

Patient → **Product** → **Process**

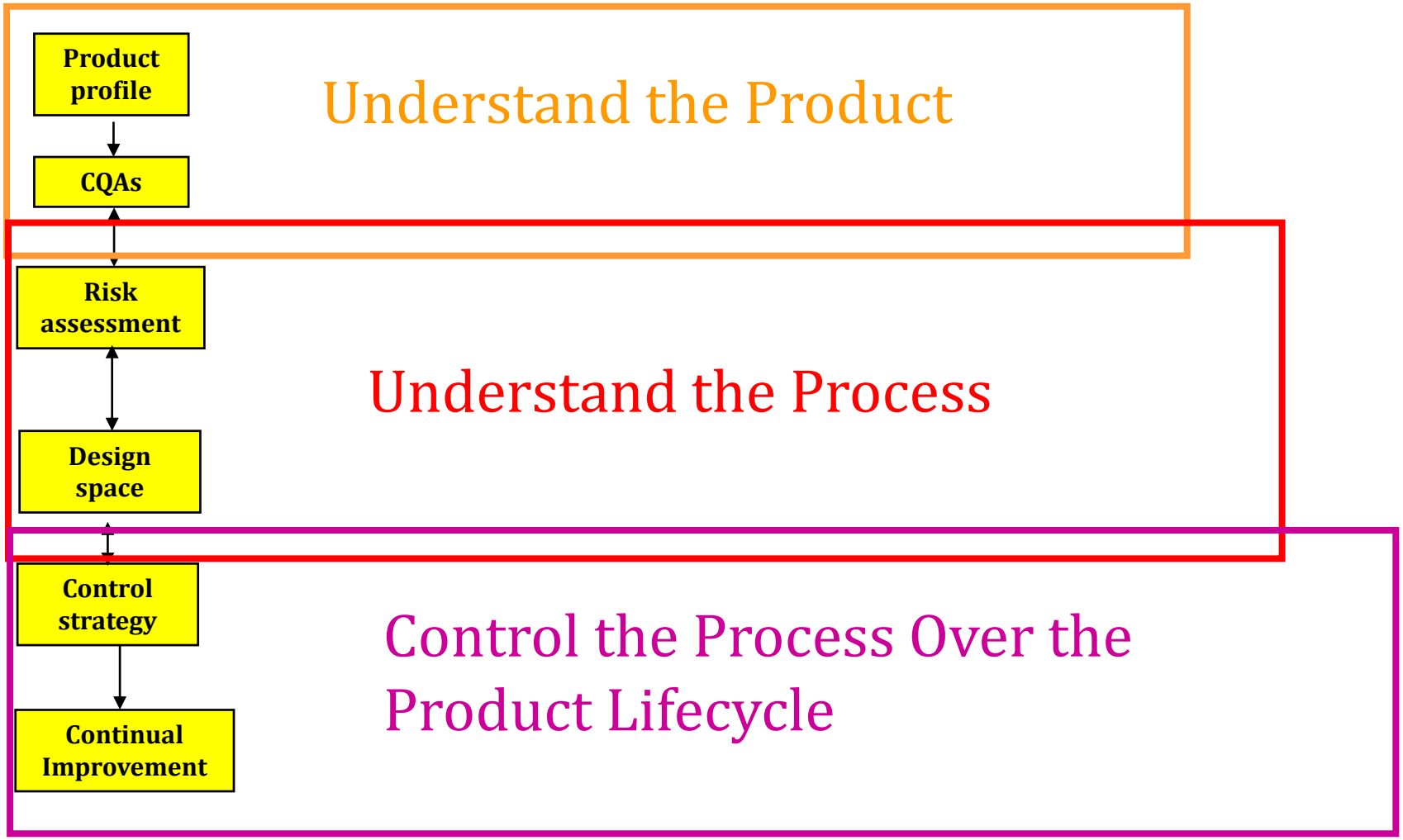
Quality Target Product Profile → **Critical Quality Attributes** → **Material Attributes & Process Parameters**

Quality by Design Approach - ICH Q8(R2)



- Target the product profile
- Determine critical quality attributes (CQAs)
- Link raw material attributes and process parameters to CQAs and perform risk assessment
- Develop a design space
- Design and implement a control strategy
- Manage product lifecycle, including continual improvement

Quality by Design Approach



"State of QbD"

- The science and risk based approaches in QbD are being embraced by most innovator pharma companies for development
- Increasingly being adopted by generics and biotech companies
- Experience has proven to improve product quality, process robustness and operational costs

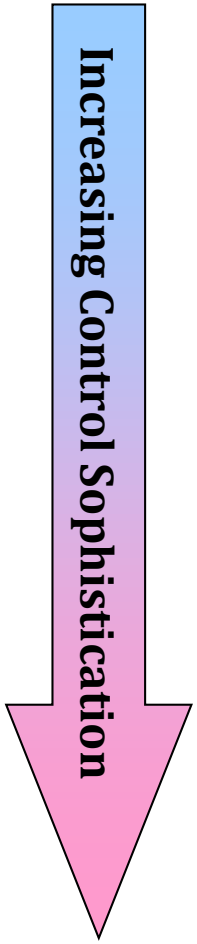
Challenges in Product Understanding (partial list)

- Solid State Formation & Characterization:
  - Ability to control uniformity of particle size
  - Manufacturing of high energy amorphous solids
  - Identity and control of solid state of active ingredient in drug product
- Biopharmaceutics Characterization:
  - Link between in vivo and in vitro performance
- Understanding the potential for misuse or abuse
  - Alcohol related dose dumping

Challenges in Process Understanding (partial list)

- Characterization and control of dynamic (path dependent) systems
  - Crystallization
  - Wet granulation
  - Lyophilization
- Understanding system dynamics of continuous manufacturing operations
  - Responses to disturbances
  - Interactions between unit operations

Challenges in Process Control



Fixed operational set points
tightly controlled raw materials

Traditional Pharmaceutical Manufacturing

Known range of allowable operation (Design Space)

Quality by Design Approach

Real-time monitoring / rapid measurements
for end point (go/no go) and release decisions

Current RTRT Approaches

Feed-back controllers

Integrated feed-forward and feedback controllers

Fully Integrated PAT (Univariate)

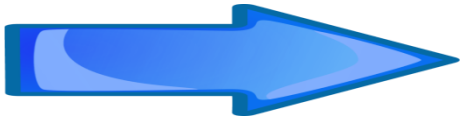
Control to a process signature
(single unit operation or plant wide)

Multivariate Control

Some Current Focus Areas

- Understanding the link from product to patient
  - Challenges of low solubility drugs
  - Integration of biopharmaceutics into QbD
- Understanding complex products and processes
  - Examples: biotech products, transdermal patches, inhalation products
- Modern manufacturing and control strategies
  - Process analytical technologies in manufacturing
  - Automated instrumentation and controls
  - Continuous pharmaceutical manufacturing

Moving Forward



- **Keep the science first!**
  - Both industry and regulators need to use science and risk based approaches
  - Good regulation follows from good science
- **Share information and experience in an open dialogue**
  - Partnerships between industry, regulatory agencies and academia
  - Broad and open dissemination of information

Thank you!

Questions, comments, concerns:

CDER-OPQ-Inquiries@fda.hhs.gov