Connecting People, Science and Regulation®

Innovation in Medicines and Manufacturing

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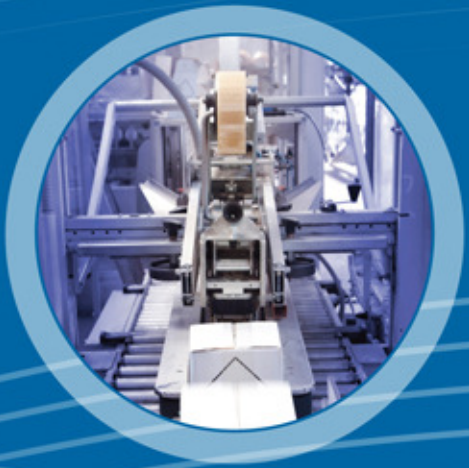


Joint Regulators/Industry QbD Workshop
28-29 January 2014 London, UK

Introduction

- Current State
  - We have heard a lot about the challenges and successes of applying QbD
  - Aside from Biopharms which we know are complex, Immediate Release Products are just the tip of the iceberg and we need to be more innovative if we are to be successful in delivering consistent and reliable quality for all products.
- Future State
  - So before we close this workshop we just wanted to reflect on some of the new challenges facing us, what could be different and to ask how do you see it?

Challenges to Innovation

- Current Levels of Technical Capability
- Availability of New Skillsets
- Unwillingness to Deploy New Technology
- Large Investment in the Current State
- Perceptions of High Regulatory Hurdles
- Lack of Process to Manage Complex LCM Changes
- Lack of an Overall Vision on How to Modernise Pharmaceutical Manufacture

Opportunities for Innovation

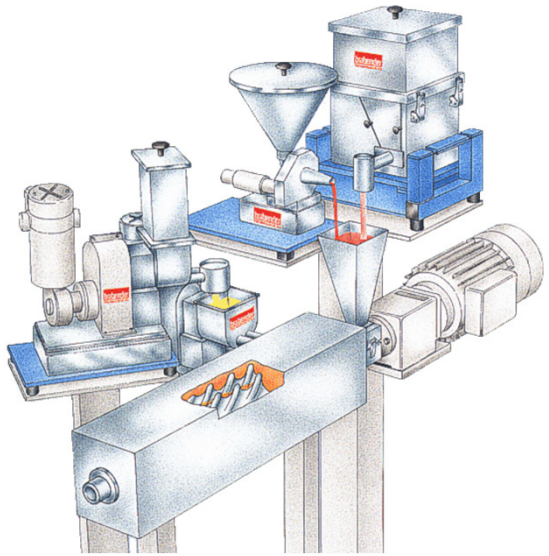
- Novel Product Types for QbD
  - More Complex Traditional Medicines
    - Prolonged release Oral, Inhaled DPI, Nanoparticulates
  - Novel products
    - Advanced Therapeutics, Oligonucleotides, Microneedles

- Novel Methods of Manufacture & Control
  - Continuous
  - Synthetic Biochemistry - Biotransformations
  - Discrete Manufacture & Novel Analytics

- Others?

Continuous Manufacturing: - Enabling Things Batch Can't Do

Benefitting
- **Quality for Patients,**
- **Environment**
- **Business**



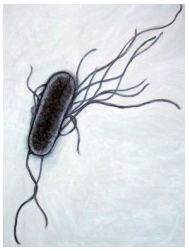
Process
- Shorter End to End Process Times
- Faster, Lower Cost Development
- More Process Understanding

Factory
- Lower Work In Progress Costs
- Safer
- More Scale Independent

Business
- Reliable Consistency
- Volume Flexibility
- Sustainable & Greener

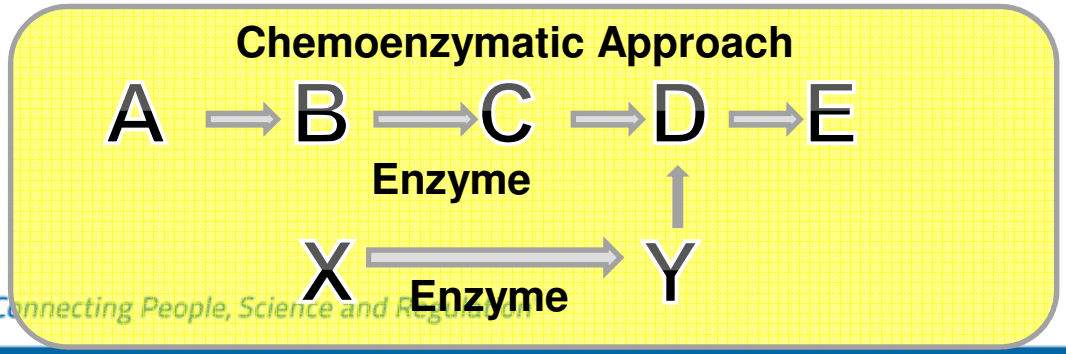
Synthetic Biochemistry

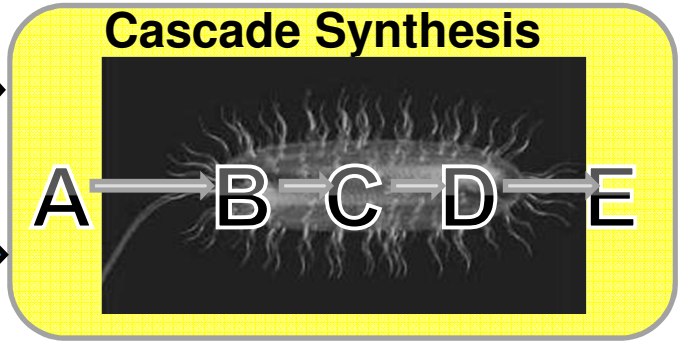
Moving to Microbial Cell Factories



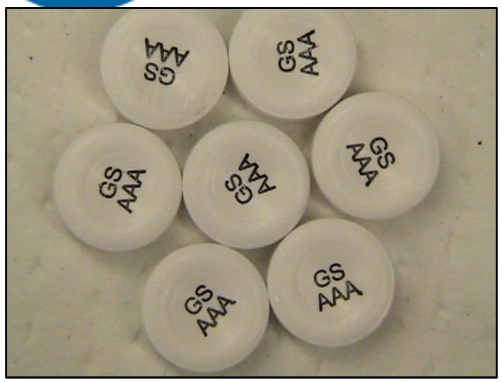
Biotransformations can be very specific in terms of chirality, position and functional group.

- **Greener, Cleaner, Cheaper**
  - **No solvents, fewer reagents**
  - **Fewer isolations & by-products**
  - **Aqueous based benign waste**





Liquid Dispensing Technology Platform

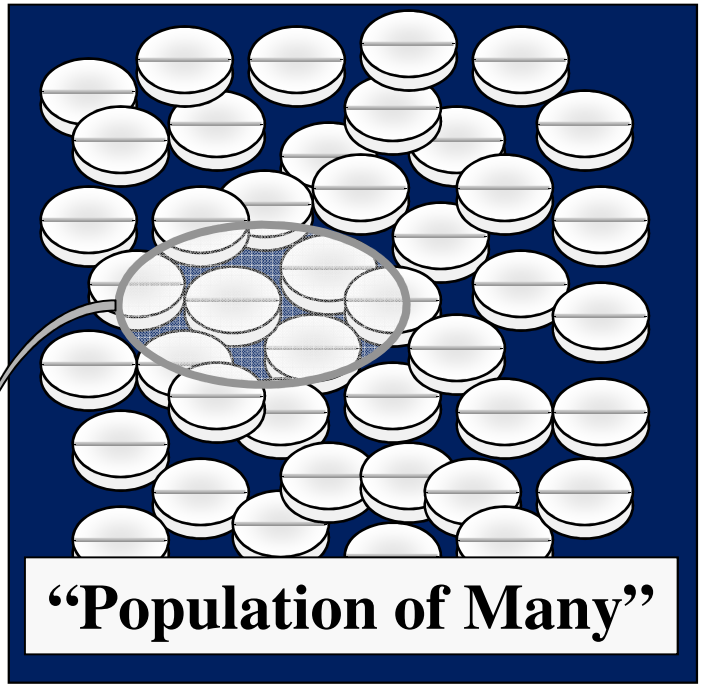


Industrial scale machine installed to provide Phase 3 and Launch Capability

Capacity: 1 million tablets/day, upgradable to 2 million/day

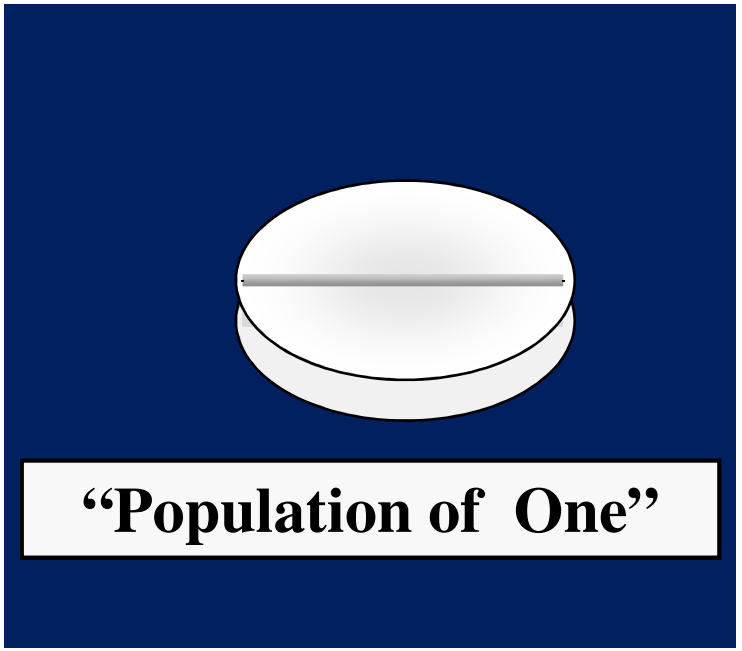
Manufacturing - A Paradigm Shift

Mfg….. Batch



Quality assessed by sampling post manufacture

Mfg….. Discrete Units



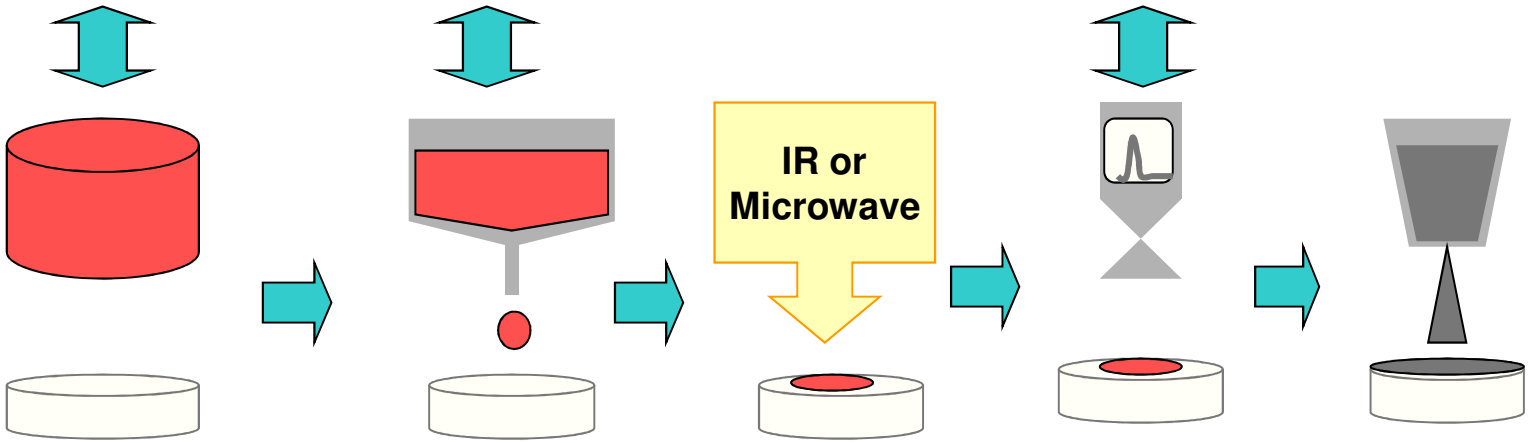
Quality assessed on-line for every tablet

Liquid Dispensing Technology with PAT

UV / NIR [suspension concentration]

1. Vision system, droplet size
2. Droplet weight

1. Image analysis
2. NIR Chemical Imaging



Drug Solution or Suspension + Placebo Tablets

Low Volume (c. 2-20ul) Dispensing

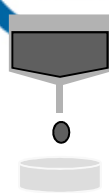
Drying

On-Line Analysis Chemical Imaging

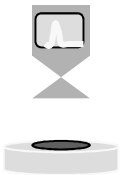
Surface Coating & Printing

No Linkage between First and Last Tablet

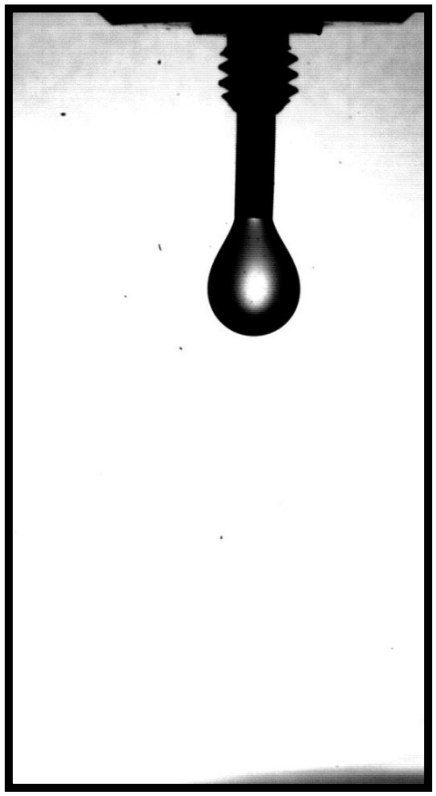
Process Analytical Technologies

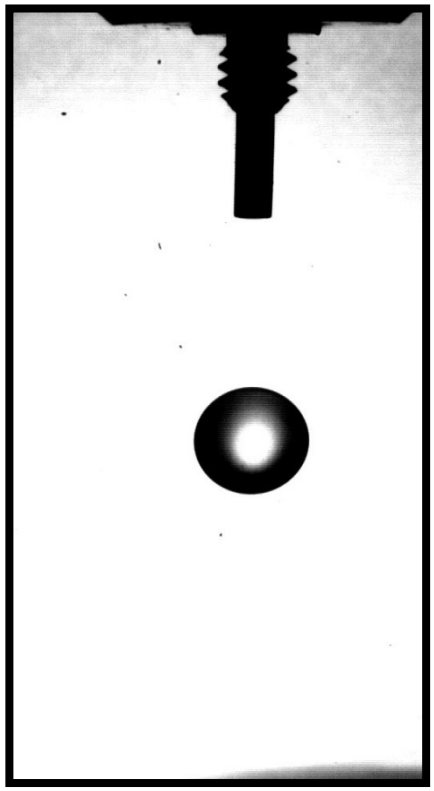


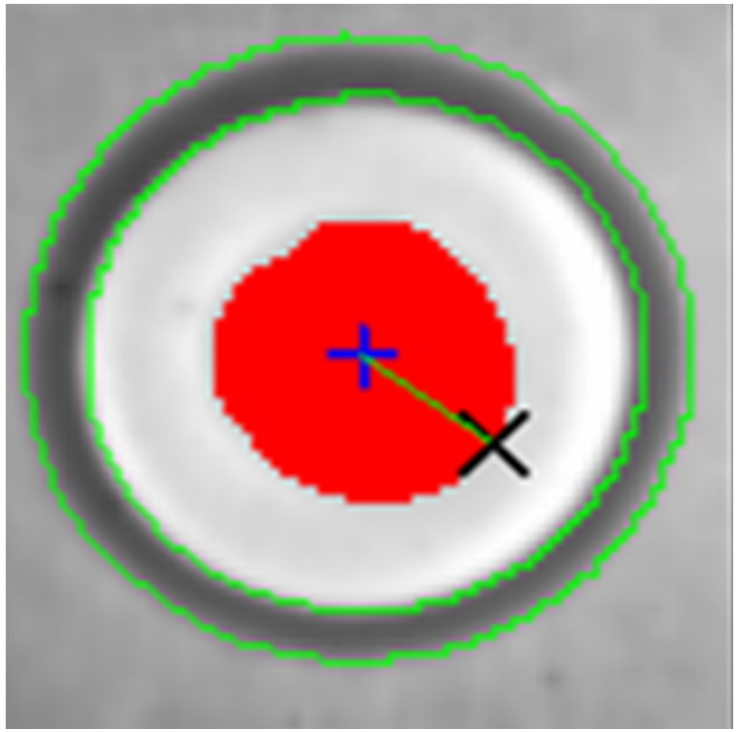
Video Image of Droplet: "What was Delivered"



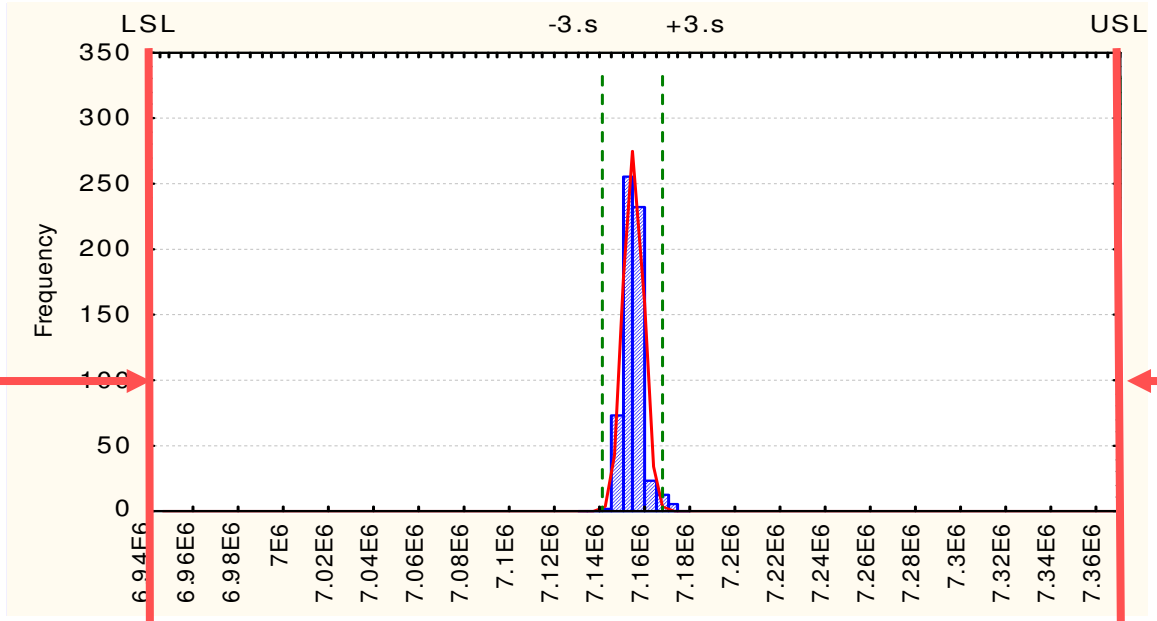
NIR Chemical Imaging: "Where on the Tablet"







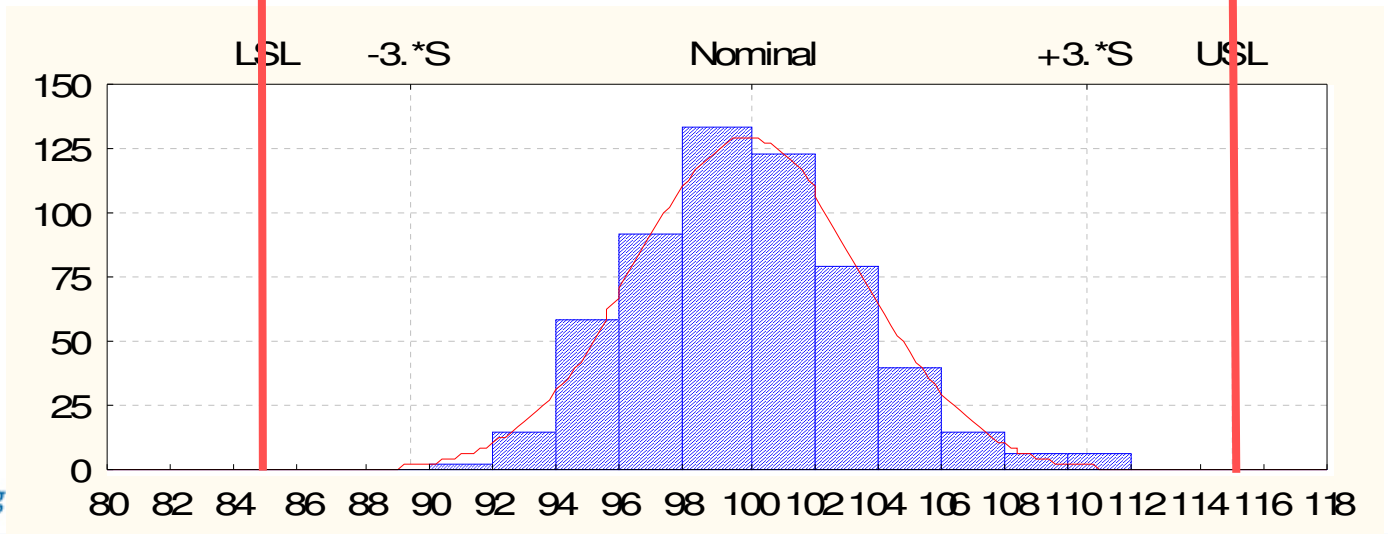
Comparison of Droplet Content Uniformity vs Typical 2mg Tablet Content Uniformity



Droplet
N= 606
PpK =16

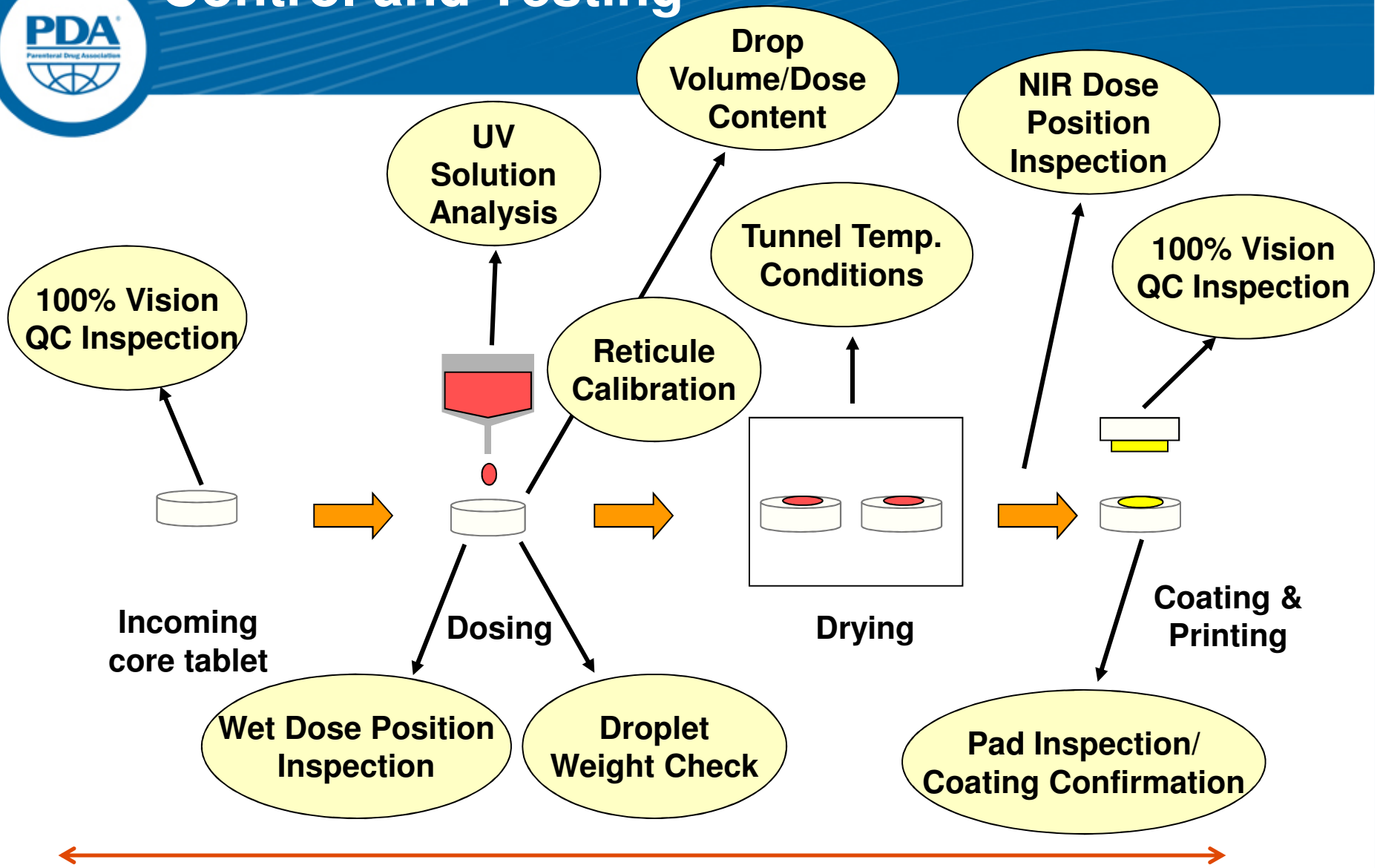
85%

115%



Tablet
N= 520
PpK =1.4

Control and Testing



Desired State

- A Vision to Modernise Pharmaceutical Manufacture
- Enabling Regulatory Strategy and Process that keeps pace with Innovation
- Increased Opportunities for Scientific Dialogue around innovative platforms
- Education and Training to Provide New Skillsets
- Enhanced scientific and risk based approaches to QbD to match new technologies
- A Simplified and Streamlined Variations Process

Challenges to Innovation

- Current Levels of Technical Capability
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Desired State

- A Vision to Modernise Pharmaceutical Manufacture
  - Industry driven

- Enabling Regulatory Strategy and Process that keeps pace with Innovation
  - Facilitate within existing Regulation

Desired State

- Increased Opportunities for Scientific Dialogue around innovative platforms
  - Scientific Advice (EMA/NCA)
  - Working Parties e.g. QWP, BWP
  - PAT team
  - early interactions recommended

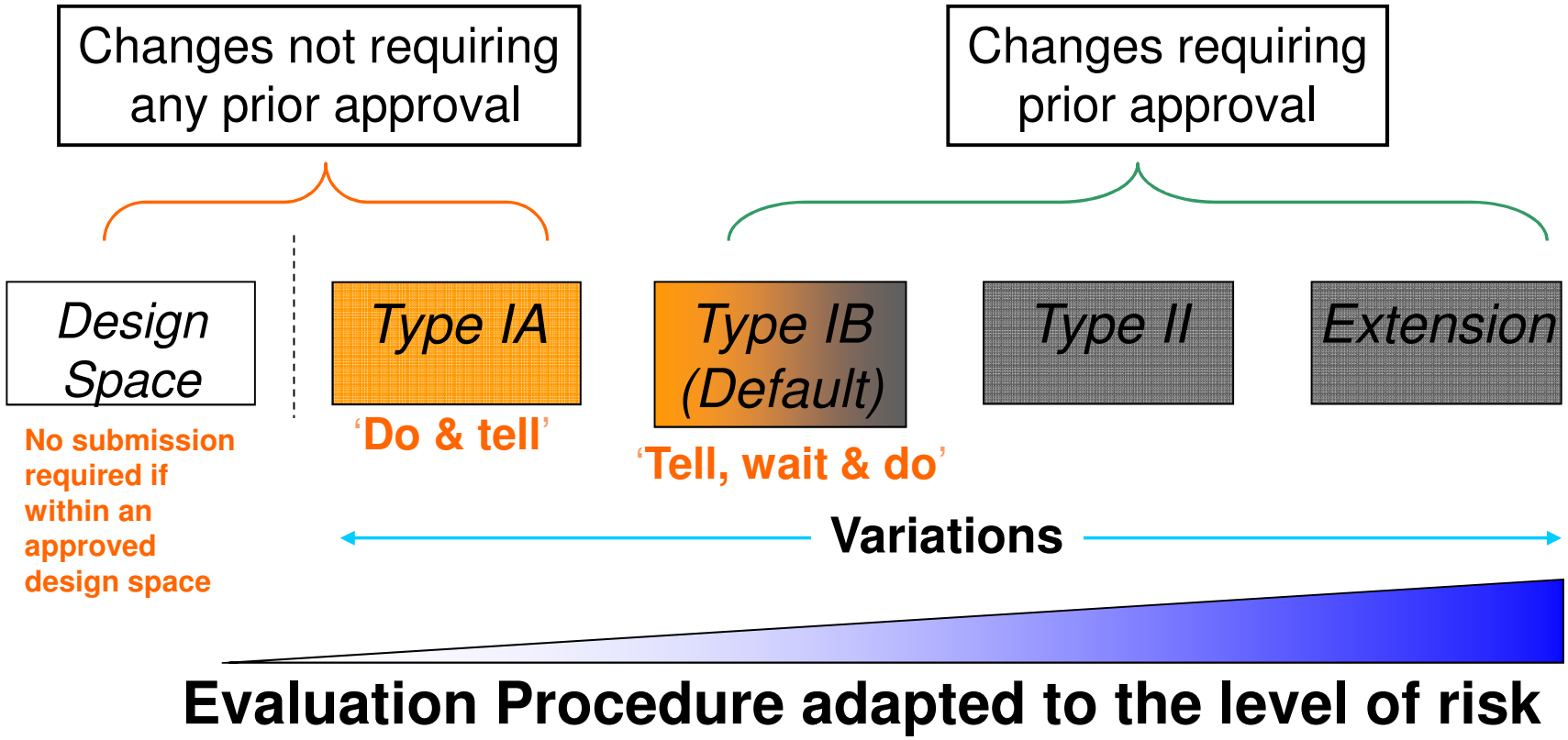
- Education and Training to Provide New Skillsets
  - Should also include Regulators

Desired State

- Enhanced scientific and risk based approaches to QbD to match new technologies
  - Apply and build on existing learning

- A Simplified and Streamlined Variations Process
  - **EU** legislation (Common system since August 2013)
  - Changes already classified on a risk based basis
  - Detailed classification guideline

Summary - Types of Variations



Desired State

- A Simplified and Streamlined Variations Process
  - EU - Changes already classified on a risk based basis
  - Additional flexibility – Post Approval Change Management Protocol (PACMP)
    - justify downgrading in type of required variation
    - no restrictions to the nature of changes
    - limit (Type IB) regarding level of downgrading for biopharmaceutical products.
  - Global challenges
  - What do you want?

Conclusion

- By No Means a Comprehensive View of the Challenges Facing All of Us or the Possible Solutions
- But a Stimulus for Further Discussion

- So How do you See the future Challenges and Opportunities for Innovation?