Accelerating the development of drug products using advanced pharmaceutical design tools and manufacturing innovation

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Overview

Drivers for change in Pharmaceutical Development

The Desired State

Advanced Pharmaceutical Design Examples

Concluding Remarks & Acknowledgements
Drivers for Change

Yesterday
- The prescriber is the key stakeholder
- Simple Distribution Channels
- Branded competition (on-patent)
- 4-6 Major Brands
- 1-2 launches/year
- Mature Markets Focus
- Primary Care Focus

Today
- Payers increasingly dominant
- Increasingly Complex Distribution Channels (inc market access)
- Branded + Generic Competition
- More Smaller Brands with multi-indications (stratification)
- 4-6 launches/year (inc. expedited programs and licensed products)
- Mature/Emerging Markets Focus
- Specialist Care Focus

Adapted from IMS Thought Leadership Presentation March 2013

QUALITY
FLEXIBILITY
SPEED
AGILITY
‘The Ambition’ - Formulation and process ready for pivotal clinical supply in <5 months with <5 kg of drug substance versus 12-24 months and from 20-100 kg for the traditional approach.

Informed risk taking through enhanced understanding

- In-Silico Formulation Design
- Accelerated & Predictive Stability Testing
- *PAT Enabled Design for Flexible Manufacture
- *PAT Enabled Technology Transfer
- In-Vitro and In-Silico Bridging

*Process Analytical Technology

Readiness for Pivotal Clinical Supply
Predicting comminution behaviour in early development

- Opportunity to predict micronisability of powders when limited amounts of material are available
- Interplanar-spacing (XRPD) could serve as a first order indicator of propensity to be micronized
- Has its limitations

Shariare et al, Pharm. Res. 2011; 29(1) 319-331
Predicting comminution behaviour in early development

Shariare et al, Pharm. Res. 2011; 29(1) 319-331

Specific interaction energy (kcal/mol/Å²)

Hardness (MPa)
Predicting comminution behaviour in early development

Interpenetrating planes providing notable barrier to lateral displacement

Shariare et al, Pharm. Res. 2011; 29(1) 319-331
Sub-optimal release linked to tablet porosity

Predicting tablet properties from composition

Accelerated Stability Assessment Program (ASAP)

Short term studies under elevated conditions designed to degrade samples and predict stability and shelf life under long term storage conditions

**Predict the effect of temperature and humidity on shelf life**

Tablet formulation at 30°C/65% RH

Continuously manufacturing potentially addresses a number of business drivers:

- **Rapid process design and optimisation**
- **Greater flexibility of batch size**
- **Greater robustness and increased consistency of product quality**
- **Minimal scale up**
- **Smaller footprint with potential for portability**
Rapid Process Design

- From weeks to days for evaluation of experimental space
- Applicable to continuous direct compression, roller compaction, twin-screw granulation and other suitable methods

*Consigma – proprietary flexible/continuous processing platform (GEA, Belgium)
Rapid Process Design

Batch Process

Increased L/S

Reduced Dissolution

Increased Adhesion

Liquid/Solid Ratio (L/S)

Predicting product performance in humans

- Advanced *in-vitro* dissolution model based on human upper GI tract (TIM-1 from TNO, Netherlands)
- Biorelevant buffers, volumes and composition
- Approximation of physiological hydrodynamics including gastric shear forces
- Simulation of passive absorption (semi-sink conditions)
- Enables determination of bioaccessible dose
Concluding Remarks

• The advantages of Advanced Pharmaceutical Design
  • Maximal Speed
  • Reduced Cost
  • Increased Quality
  • Increased Flexibility
  • Increased Agility

• Notable impact already demonstrated for aspects of Advanced Pharmaceutical Design

• The stage is set for consolidation of tools into a framework for product and process design to enable the accelerated development and approval of new medicines
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