Pharmaceutical Development Services

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

Marcel de Matas

Seda Pharmaceutical Development Services®
The Biohub at Alderley park
Alderley Edge
Cheshire SK10 4TQ
marcel.dematas@sedapds.com
www.sedapds.com

INTERNATIONAL MULTIDISCIPLINARY SYMPOSIUM ON DRUG RESEARCH & DEVELOPMENT
IN MEMORY OF PROFESSOR ÜNSAL ÇALIŞ

Overview

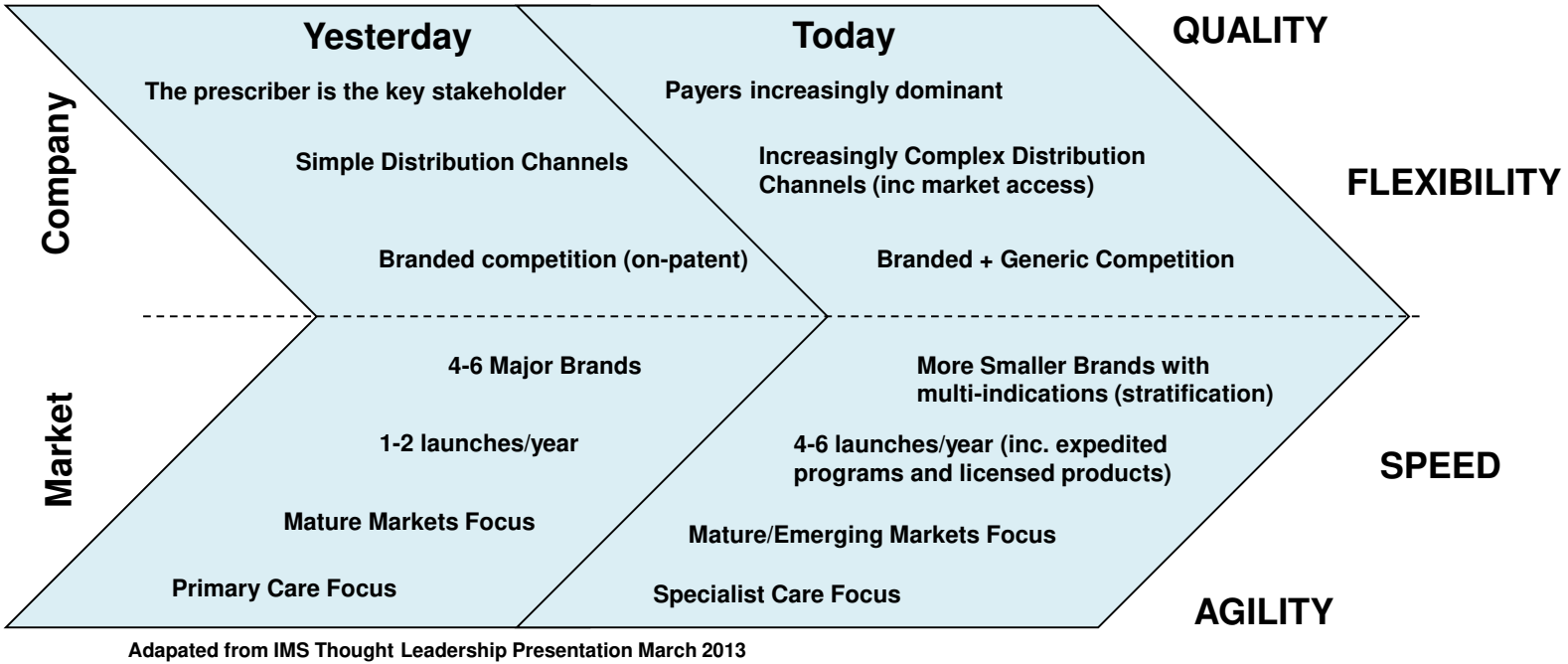
Drivers for change in Pharmaceutical Development

The Desired State

Advanced Pharmaceutical Design Examples

Concluding Remarks & Acknowledgements

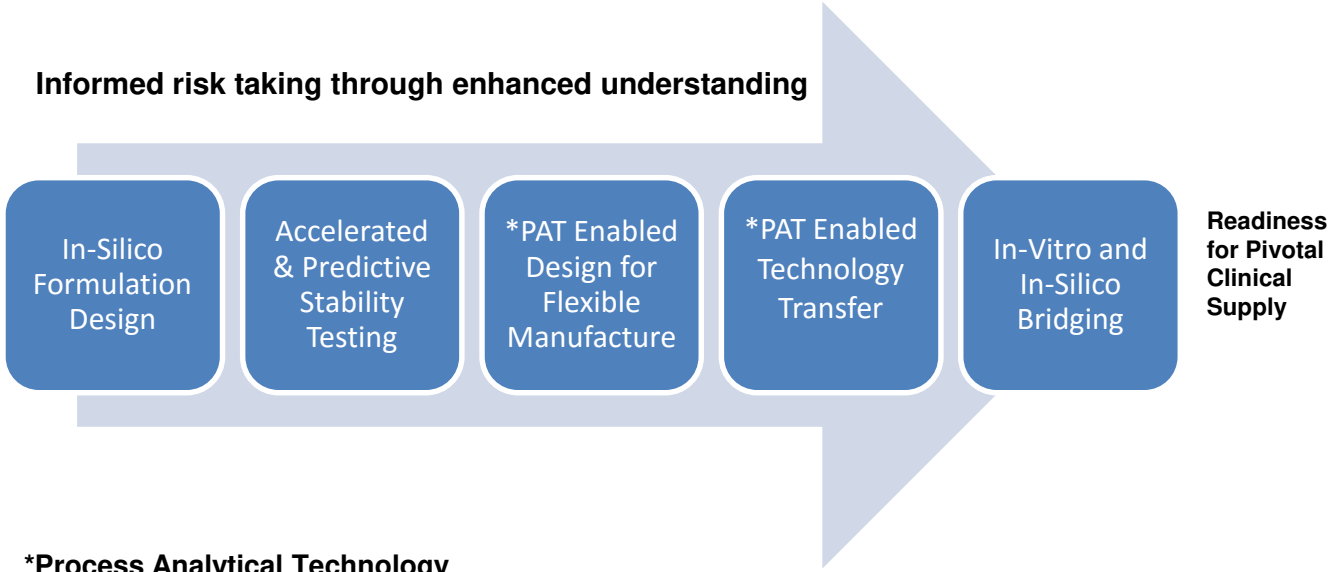
Drivers for Change



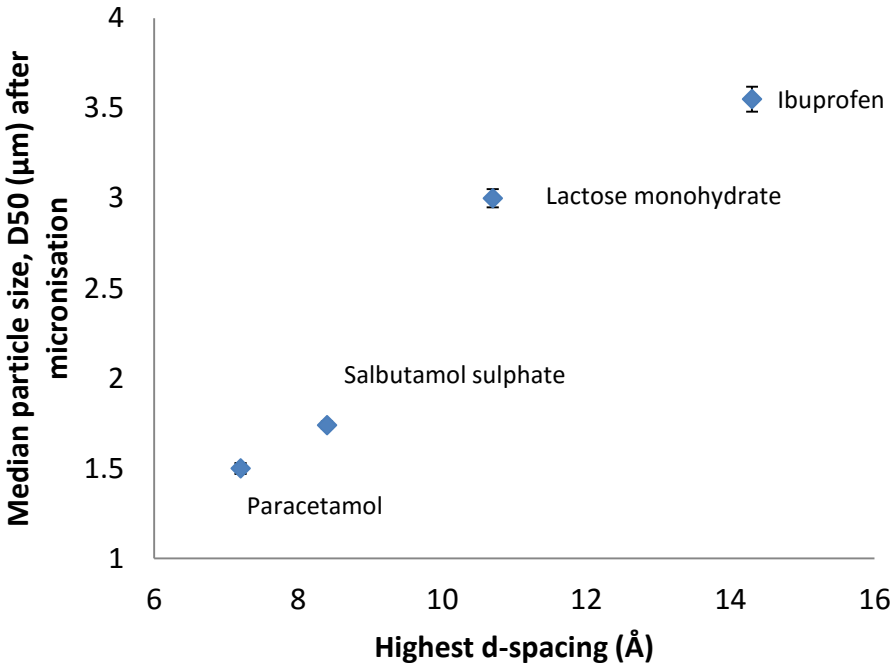
Adapated from IMS Thought Leadership Presentation March 2013

The Desired State – Advanced Pharmaceutical Design

- ‘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.



Predicting comminution behaviour in early development



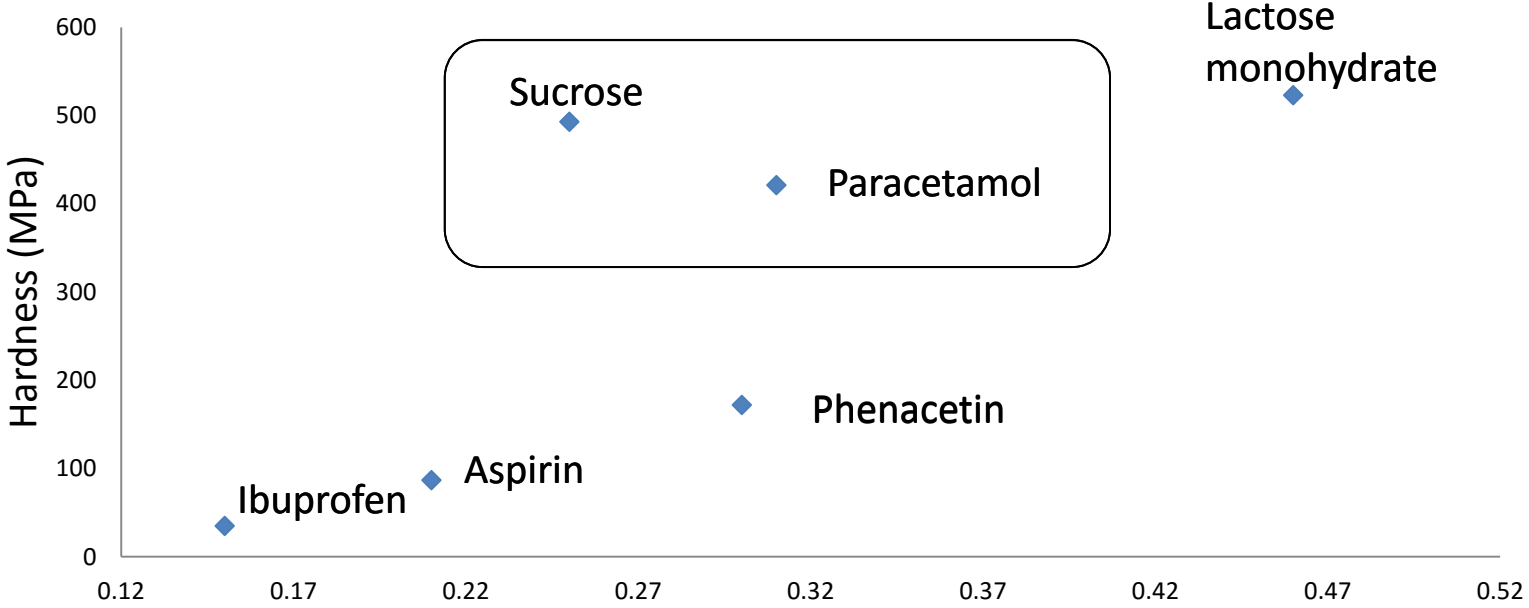
- Opportunity to predict micronisability of powders when limited amounts of material are available

- Interplanar-spacing (XRPD) could serve as a first order indicator of propensity to be micronized

- Has its limitations

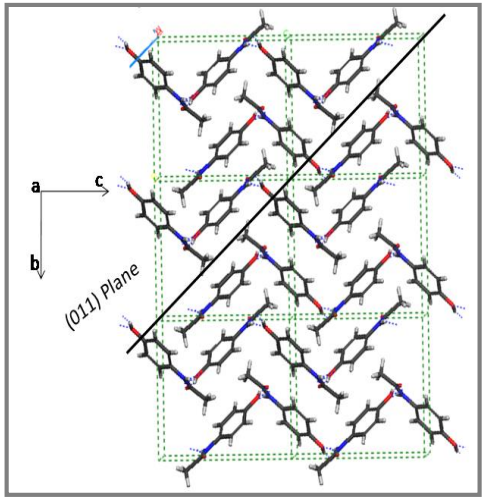
Shariare et al, Pharm. Res. 2011; 29(1) 319-331

Predicting comminution behaviour in early development

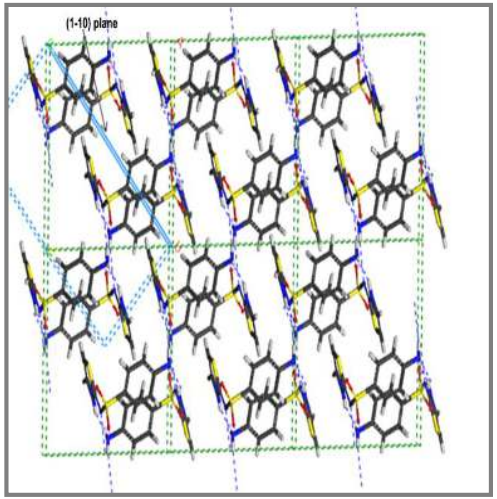


Shariare et al, Pharm. Res. 2011; 29(1) 319-331

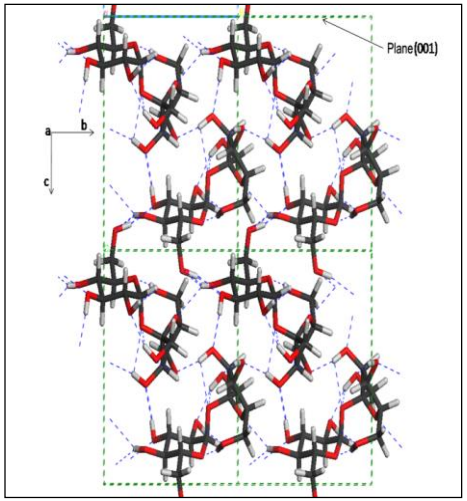
Predicting comminution behaviour in early development



Paracetamol



Sulfathiazole



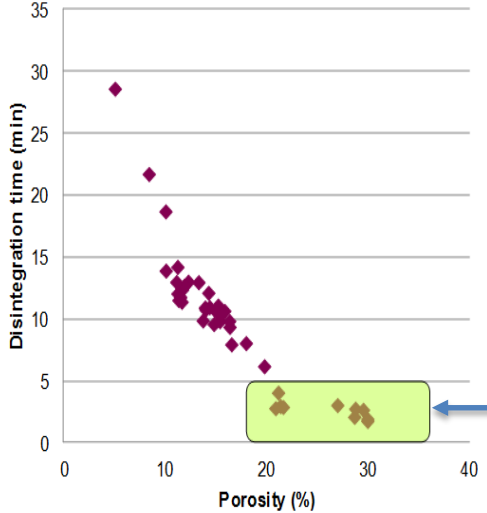
Sucrose

Interpenetrating planes providing notable barrier to lateral displacement

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

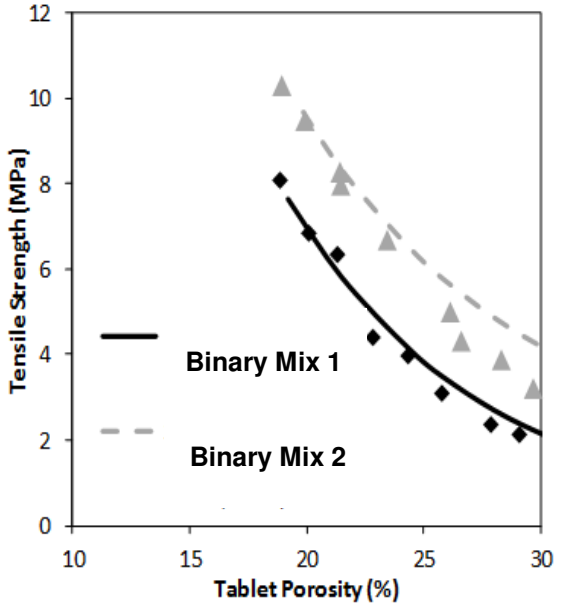
Rapid Tablet Design

Sub-optimal release linked to tablet porosity



Good Dissolution

Predicting tablet properties from composition

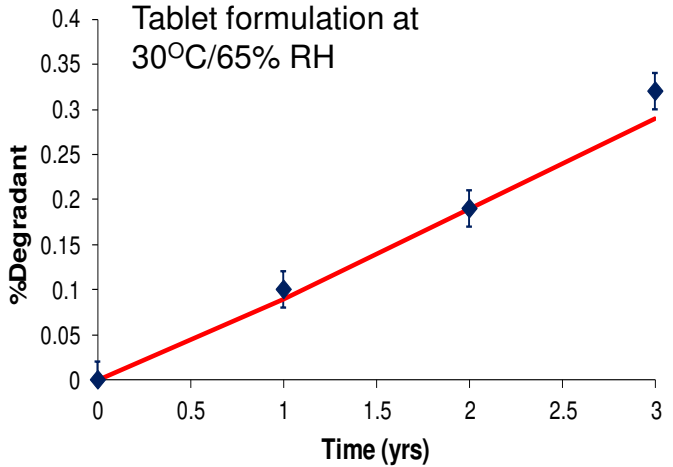


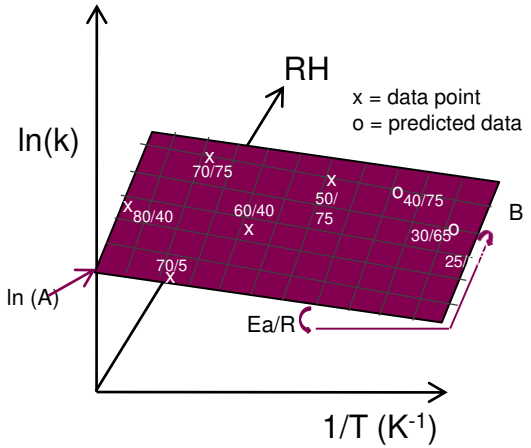
Relevant references: Wu et al, Pharm Res. 2006; 23(8) 1898-1904; Gavi & Reynolds. Comp. Chem. Eng. 2014; 71 130-140

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

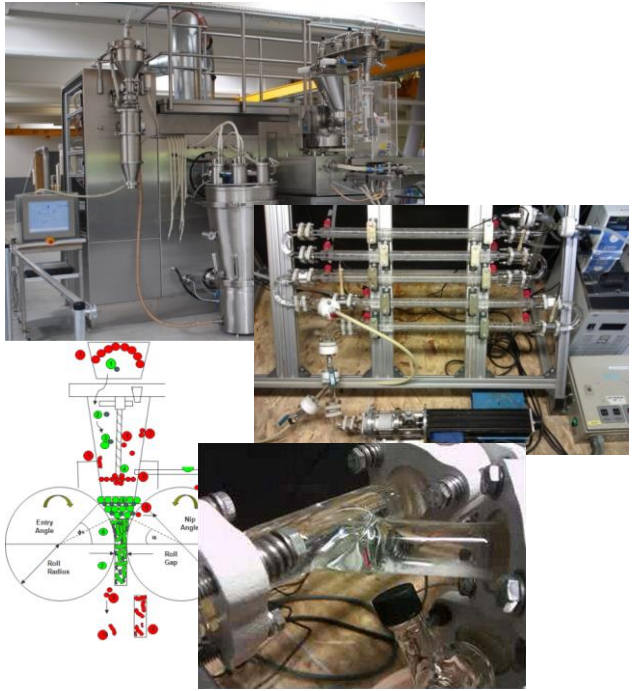
Predict the effect of temperature and humidity on shelf life





Based on methods described by KC Waterman, AAPS PharmSciTech. 2011; 12(3): 932–937.

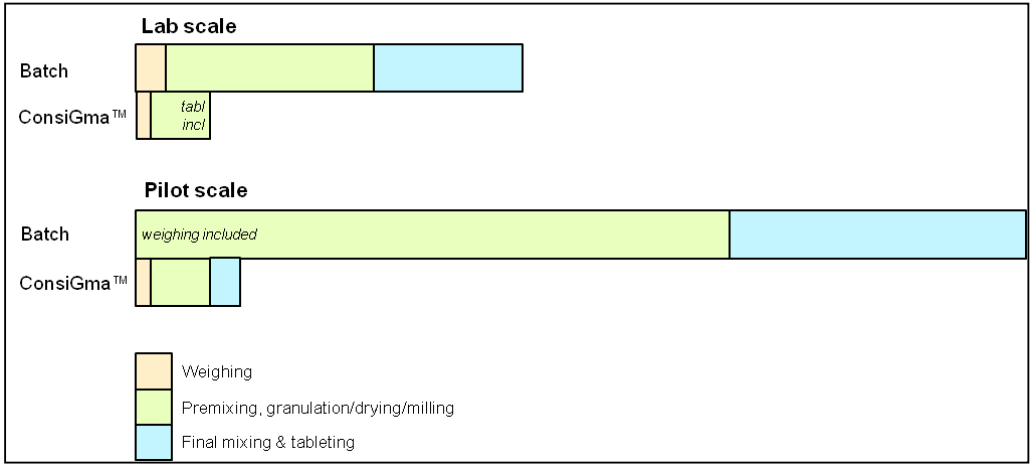
The 21st Century Supply Chain – Continuous Manufacture



- **Continuous 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

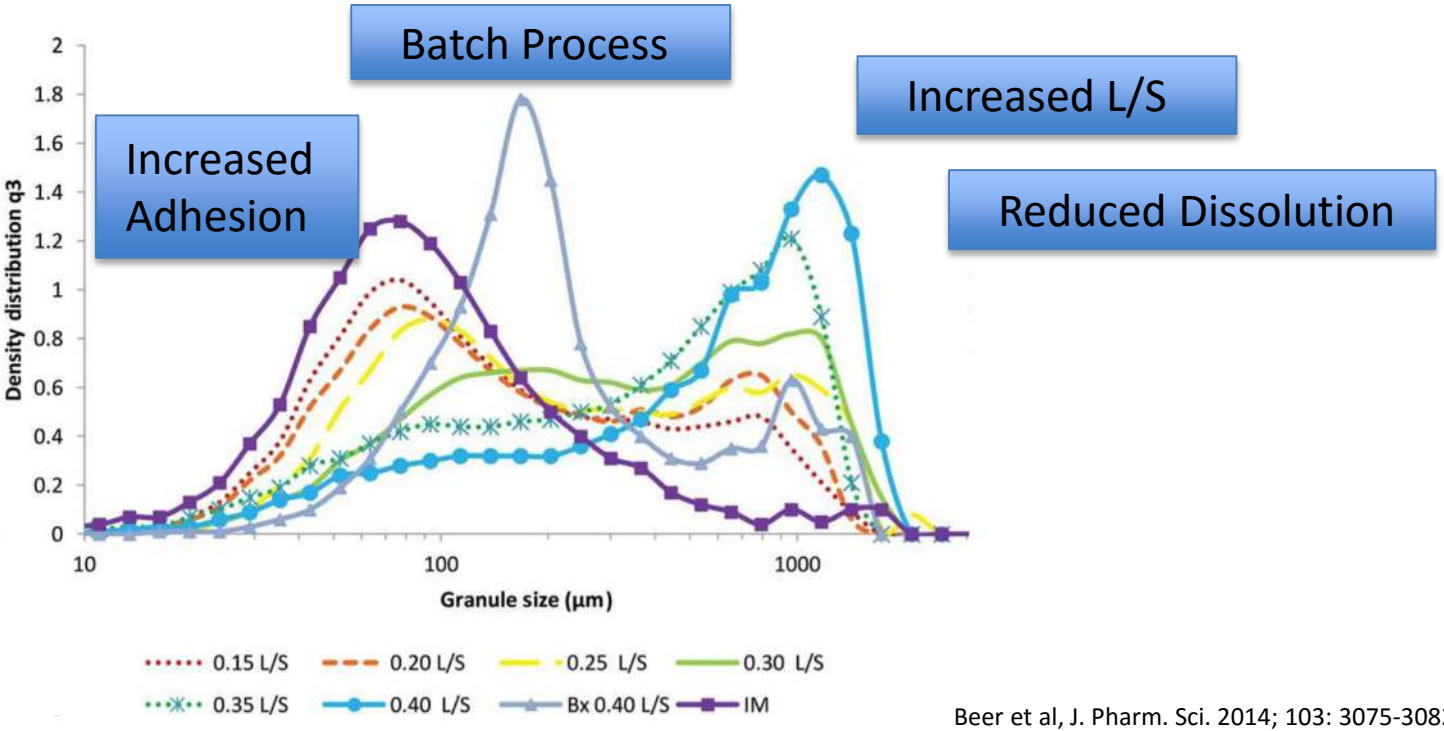
Rapid Process Design

- 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



Liquid/Solid Ratio (L/S)

Beer et al, J. Pharm. Sci. 2014; 103: 3075-3082

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

Acknowledgments

- Mohammad Shariare
- Jamshed Anwar
- Frank Leusen
- Peter York
- Paul Beer
- David Wilson
- Zhenyu Huang
- Gunnar Haeffler
- Pirjo Tajarobi
- Staffan Folestad

Paul Dickinson
Claire Patterson
Richard Barker

Pharmaceutical Development Services

DRD 2015

October 17th 2015