CAMP

Consortium for the Advancement of Manufacturing in Pharmacy
Original Vision

- Develop the manufacturing system for the 21st century
- Disposable Modules
- Project Metrics
  - 100% Forecast turnover in 3 days
  - 48 hour cycle time
  - on-line validation
  - parametric release
  - paperless factory
Chronology

- 1992/3 - Planting the seed
  - Future search
  - Facilities 2001 meeting at MIT
  - MIT Liaison meeting at Roche

- 1993/4 - Germination
  - Sigel networking
  - Facilities 2001
  - MIT
  - Purdue invited to join the effort
Chronology Continued

- 1995 - Fertilization
  - Feb - Organizational meeting at Cambridge/MIT
  - Jun - Industry meeting at Nutley
  - Aug - Planning meeting at Cambridge
  - Dec - Kickoff meeting at Cambridge
Chronology Continued

- 1996 - Sprouting
  - Feb - Implementation meeting at Arlington
  - Apr - Initial steering meeting at New York
  - Jun - Steering meeting #2 at Radnor
  - Jul - Steering meeting #3 at Morris Plains
  - Sept - Steering meeting #4 at Indianapolis
  - Nov - Steering meeting #5 at Nutley

- 1997 - Growth - Quarterly meetings
CAMP Mission

The Consortium for the Advancement of Manufacturing in Pharmaceuticals (CAMP) is dedicated to the identification, research, and development of new manufacturing technology.

Our objective is to improve healthcare delivery by lowering product costs and decreasing new product time-to-patient.
Founding Concepts

- Research-Based firms committed to manufacturing R&D in both chemicals and pharmaceuticals
- Resolve long-standing issues
- Achieve break-through technological developments
- Focus on sensors and sensor development
- Achieve FDA acceptance
- Significantly improve
  - Cost-of-goods
  - Time-to-market
Business Drivers

- Regulatory
- Political – cost and availability of medicines
- More complex products and pipeline
- Technology: Outdated, inefficient, variable results, not well understood
- Skills: Limited availability of technical experts
Organization

- Original Membership - Abbott, Hoffmann-LaRoche, Johnson & Johnson, Rhone-Poulenc Rorer, Smith-Kline Beecham, Warner-Lambert, and Wyeth Ayerst
- Current Membership - Abbott, Hoffmann-LaRoche, Johnson & Johnson, GSK, Novartis, BMS, Sanofi-Aventis, and Wyeth Ayerst
- Funding
  - Dues - $150,000 per year
  - Project funding P.R.N.
Organization

- Directors
  - G.K. Raju
  - Bill Leishear

- Universities
  - Purdue - Steve Byrn - IPPH

- Non-profit organization
Project Selection Process

- Long list of projects submitted and reviewed
- Develop short list by voting and ranking
- Project proposals requested
- Fund - IND, Alpha, and Beta Phases
- Partner with universities and vendors
Initial Projects

- End point of drying
- Homogeneity of dry powder blends
- Rapid microbial detection
- Rapid sampling valve
Current Projects

- Roller compaction
- High shear wet granulation
- Coating
- Computational cluster
- Acoustic for Tablets
- Sensor design
Coating Project

Purdue University
Prof. Ken Morris
Prof. Carl Wassgren
Prof. Paul Sojka
Jose D. Perez-Ramos
Vincent Hoon

Technical Champion: GSK
Shawn Whitfield
Keith Hill
The long range objective of this project is to model (design) and monitor the (functional) film coating process for tablets in a coating pan, to determine endpoint and variability, for significant process control and development / manufacturing benefits.
Goals

NIR Sensor Development and Application

Purpose: NIR diffuse reflectance sensors will be used to monitor the inter- and intra-tablet uniformity during the coating process so that the process can be controlled.

Significant Tasks:
- NIR-film thickness calibration
- Univariate and multivariate analysis tools and strategies (chemometrics)
- Signatures for core vs. coating signals
- Measure face vs. band coating growth
- Confirm in-line sensor performance and reproducibility.
- Determine from the DEM simulations what factors might affect the NIR sensor measurements and also determine the optimal location of the sensor
Goals 2

DEM Dynamics Modeling

Purpose: Predict the kinematics and dynamics of biconvex tablets in a horizontal pan coater, as a function of tablet size distribution, shape, and material properties, drum geometry and speed, baffle configuration, pan fill level, and drying air flow rate. The models will also predict the uniformity of the conditions (e.g. time spent in the spray zone and force distributions) experienced by individual tablets.

Significant Tasks:
- model tablet/tablet and tablet/pan contact forces using the “soft particle” approach
- model 2D and 3D motion
- include several tablet geometries including spheres, “glued sphere” biconvex tablets, and “intersecting glued sphere” biconvex tablets
- create a visualization tool for displaying the simulation results
- define the degree of tablet orientation so that quantitative comparisons can be made regarding the coating spray coverage on the tablet bed
- design the procedure for making measurements within the simulation of parameters including velocities, orientation, forces, and durations spent in particular regions of the tablet bed
- model complex pan geometries and baffle configurations
- include aerodynamic force effects
- validate the simulations against experimental measurements of tablet orientation at the bed surface and tablet coating growth rates
Spray Modeling

*Purpose:* Predict and measure the dynamics of the coating spray for improved process design. The models and measurements will be incorporated into the DEM models in order to predict the growth rate of individual tablets. Tablet growth rates will be a function of position, speed, and orientation within the tablet bed (predicted by the DEM simulations) as well as spray patternation and efficiency (predicted by the spray models).

*Significant Tasks:*
- measure spray drop size and velocity distributions for use in the DEM models
- model drop velocities and trajectories including aerodynamic effects
- measure surface patternation for use in the DEM models
- predict droplet rebound probabilities
- predict spray transfer efficiency
- investigate the influence of tablet bed curvature effects
- investigate the influence of tablet bed roughness
- incorporate spray models into the DEM models to predict tablet coating growth rates
Spectra collected on one Coating Experiment

- HPMC (~1734 nm)
- Water (~1934 nm)
- Sulfanilamide (~1967 nm)
Preferred Orientation Index, $\sigma$

- Define the orientation index so that \textit{varies linearly} with the band-to-cap area ratio, and so $\sigma = 1$ gives the ideal, or desired, orientation:

$$\sigma \equiv \frac{B/C_{\text{measured}}}{B/C_{\text{ideal}}}$$

- $\sigma < 1 \Rightarrow$ more cap than desired
- $\sigma = 1 \Rightarrow$ ideal
- $\sigma > 1 \Rightarrow$ more band than desired

- For the current tablets: $B/C_{\text{ideal}} = B/C_{\text{total}} = 0.58$

- Special cases:
  - Only caps exposed: $B/C_{\text{all caps}} = 0 \Rightarrow \sigma_{\text{all caps}} = 0$
  - Maximum $B/C$: $B/C_{\text{max B/C}} = 3.90 \Rightarrow \sigma_{\text{max B/C}} = 6.72$

Note that the special case values for $B/C$ will vary depending upon the tablet geometry.
Effect of Inlet Air Presence on Preferred Orientation Index
(10 pt. Band/Cap ratio Moving Average, ~0.5 Pan Revolution)

Orientation Index ($\sigma$)

% Revolution

8 RPM, Inlet Air ON
10 RPM, Inlet Air ON
12 RPM, Inlet Air ON
14 RPM, Inlet Air ON
16 RPM, Inlet Air ON

10-point Average Smoothing
7 Kg load, Baffles On
Effect of RPM and Pan Load on $\sigma$
(10 pt. Band/Cap ratio Moving Average, ~0.5 Pan Revolution,
Baffles ON, Inlet Air ON)

Orientation Index ($\sigma$)

- Blue = 7 kg Pan Fill Load
- Red = 5 kg Pan Fill Load
- Green = 3 kg Pan Fill Load
Growth Rate Measurements

Coating Materials:
- HPMC (Grade E3) : 10% coating suspension
- PEG 6000 : 1% coating suspension

Coating Experiment Parameters:
- Pan fill load: 7 kg
- Pan speed: 12 rpm
- Spray rate: 50 ml/min
- Atomization pressure: 30 psig

From video experiments:

\[
\frac{B}{C} \bigg|_{\text{Measured}} = 0.18 \\
\frac{B}{C} \bigg|_{\text{Ideal}} = 0.58
\]

\[
\frac{t_B}{t_C} \bigg|_{\text{Predicted from video experiment}} = 0.62
\]

From tablet coating experiments:

\[
\frac{t_B}{t_C} \bigg|_{\text{Measured from coating experiment}} = \frac{0.8855}{1.1649} = 0.76
\]
Movie – DEM Simulation
Conclusion

- CAMP is a leading manufacturing research organization
- CAMP does research that is too expensive for an individual company to carry out
- CAMP carried out research that led to the establishment of FDA’s PAT initiative
- CAMP will evolve to increased emphasis on sensor- manufacturing device interface