

Addressing Drying Challenges in the Pharmaceutical Industry

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Outline

- Introduction of ETC Drying Working Group
- Objectives of Drying WG
- The ETC Collaboration Process
- Progress Toward Project Implementation
- Summary



ETC-Drying Working Group Background

- Formed in January, 2015 and is presently active
- Consists of members representing 10 pharmaceutical companies

Company	Team Member(s)
AbbVie	Jerry Gaertner
Amgen	Andrew Cosbie, Seth Huggins
AstraZeneca	William Hicks, Claire MacLeod
Boehringer Ingelheim	Fredrik Nordstrom, Bing-Shiou Yang
Bristol-Myers Squibb	Eric Saurer, Kathryn Camacho, Joshua Engstrom
Elli Lilly	Ed Conder, Kevin Seibert
Merck	David Lamberto
Pfizer	Mark Maloney
Takeda	Charles Papageorgiou
Genentech	Archana Kumar, Lady Mae Alabanza



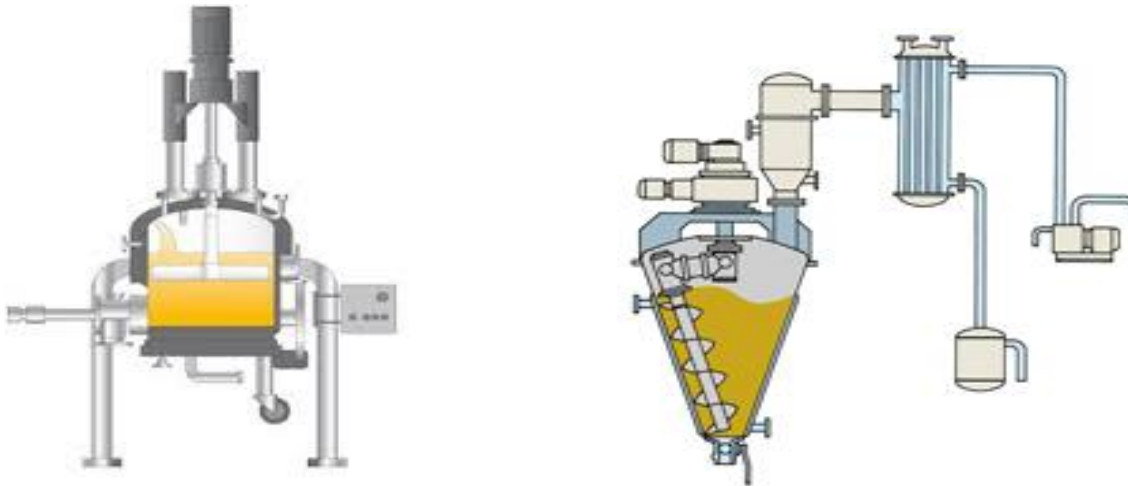
Why is the Drying WG needed?

- **Drying of pharmaceutical drug substances is complex**
 - API in particular must meet many quality attribute criteria (crystalline form, powder properties, residual solvent content, purity)
- **Impact of process parameters in dryers on drug substance is not fully understood**
 - Predicting outcome of DS QAs for scale-up and tech transfer is difficult, especially when material quantities are limited
 - Scale-up and tech transfer is largely based on empirical understanding
- **There are several gaps in process development understanding**
 - Equipment technology
 - Experimental and computational modeling
 - No unified guidance on work flow for development



Drying WG Objectives

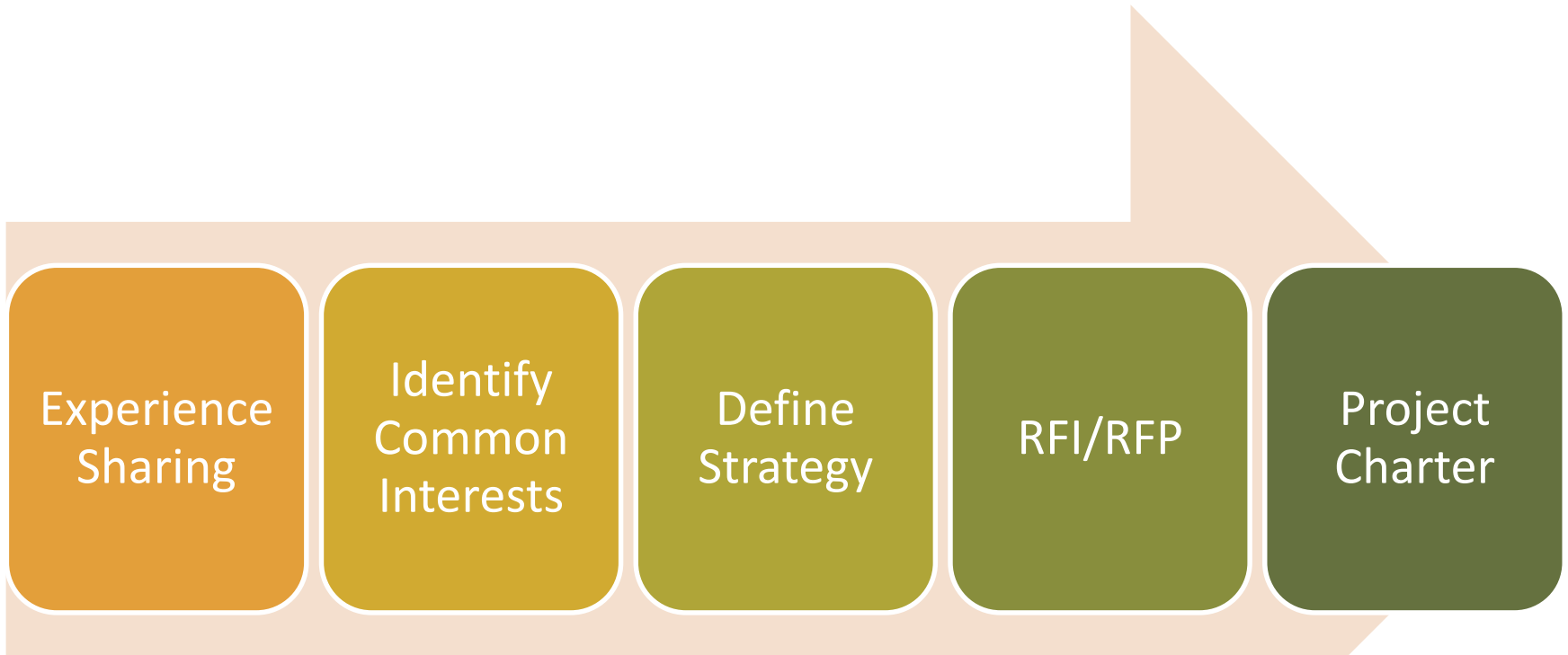
- Identify technical improvement opportunities for drying process development and understanding
- Focus on common drying interests



<http://www.mixers.com>



Collaboration Process



Process used to manage competing priorities and interests to find common projects of interest to all sponsor companies



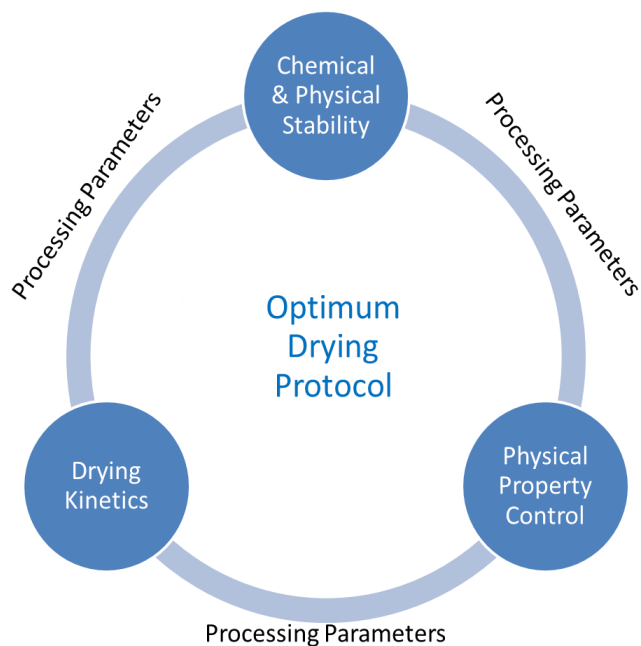
Experience Sharing and Common Interests

- **Each participating company presented on drying practices and development approaches**
- **Common interests from all presentations included:**
 - Better design of scale-down equipment
 - Improved modeling
 - Improved PAT for real time data collection and materials sampling/characterization



The Challenge of the Drying Unit Operation

- The elements of drying (chemical/physical stability, drying kinetics, powder prop. control) are interrelated
- Designing a robust drying protocol requires understanding of critical process parameters that have impact on all the drying elements



ORGANIC PROCESS RESEARCH & DEVELOPMENT

OPR&D

Review

pubs.acs.org/OPRD

The Pharmaceutical Drying Unit Operation: An Industry Perspective on Advancing the Science and Development Approach for Scale-Up and Technology Transfer

Edward W. Conder,[†] Andrew S. Cosbie,[‡] John Gaertner,[§] William Hicks,^{||} Seth Huggins,[‡] Claire S. MacLeod,^{||} Brenda Remy,[¶] Bing-Shiou Yang,[#] Joshua D. Engstrom,^{*,¶} David J. Lamberto,^{*,¶} and Charles D. Papageorgiou^{*,¶}

Org. Process Res. Dev. 2017, 21, 420–429



Strategy for Technological Improvements

- **1st: Focus efforts on real-time data collection in agitated dryers (e.g. PAT) at all scales**
- **2nd: Build improved drying models on basis of data collection**
- **3rd: Design appropriate scale-down equipment to more accurately predict scale-up or tech transfer issues when material is limited**

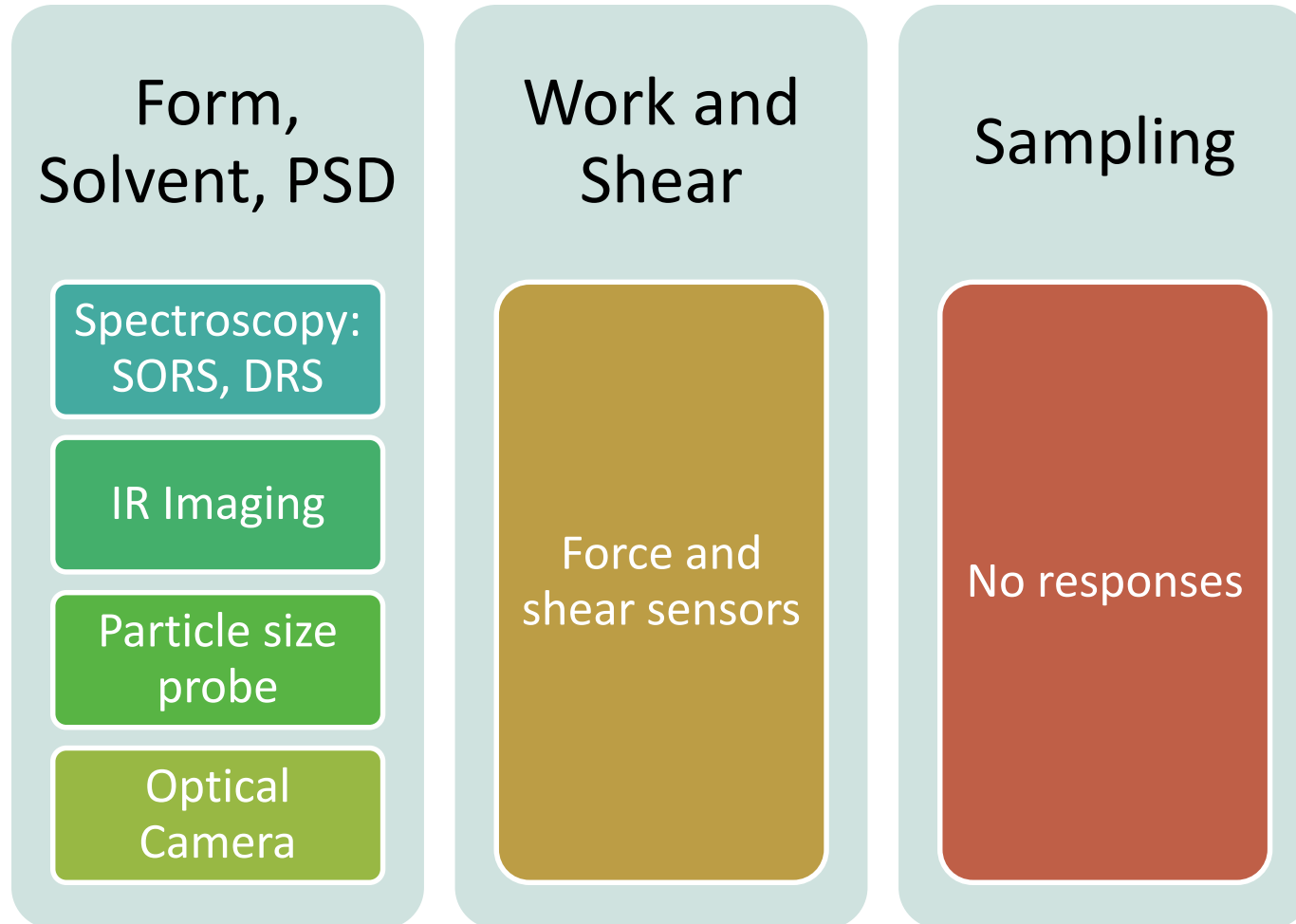


RFI on Real-Time Data Collection: Desired Capabilities

- **Real-time measurements of solvent composition, polymorphic form and/or particle size distribution.**
 - Interest in non-contact PAT technologies (e.g. sonar)
 - Ability to measure larger “spot” areas and/or 3D profiling
- **Measure work and shear**
 - Ability to “measure” shear experienced by particles along the impeller/agitator of the dryer to understand impact to particle size
- **Sampling from the dryer at Lab and Pilot Scale for off-line testing**
 - Enable automated sampling during drying in agitated dryers without breaking vacuum
 - Method to retrieve representative samples during drying



RFI Responses



6 responses received



Evaluation of RFI responses to prepare RFP(s)

Categories	Weighting	Spectrosc. Option 1	Spectrosc. Option 2	IR Imaging	Optical Camera	Particle Size Probe	Force and Shear Sensors
Cost	1	1	2	2	3	2	1
Develop. Time	1	1	2	2	3	1	1
Impact	5	3	3	2	1	2	2
Prob. of Success	3	2	3	2	2	3	2
Total Score: (sum product of Weighting x Risk)		23	28	20	17	22	18

➤ Team analysis indicated that spectroscopy responses would be pursued for further RFP



RFP: Development of spatially resolved spectroscopy probe for application in pharmaceutical drying processes

- Design and development of a probe or probe-like instrument with integrated optics for the application of spatially resolved spectroscopy (e.g. IR and/or Raman) in agitated vacuum contact dryers to profile the drying process throughout the vessel
- Development of spectral analysis methods, models, and calibrations to determine solvent content, physical form, and particle size distribution across a range of conditions



Spectroscopy RFP Status Update

- **2 responses (same respondents from RFI, but with additional details)**
- **Vendor selection is ongoing**
- **Next step: Charter preparation**
 - Dependent on member company interest
 - Will need to weigh value of investment against advancement in development



The Strategy Implementation Continues

Real-time (PAT) measurement projects

Spectroscopy project evaluation in progress

Drying group still interested in pursuing new PAT projects

Modeling RFI/RFP

To be initiated in 2018

To be done in parallel to PAT projects

Scale-down projects

To be initiated upon findings from PAT and modeling work



Summary

- **Drying WG has been active since early 2015**
- **Published paper highlights industry perspective on challenges and issues in the development of drying processes**
- **Currently executing strategy outlined in paper**
 - Spectroscopy RFP in process
 - Modeling RFI/RFP underway
 - Scale-down equipment approach being considered
- **Further information can be found at: www.etconsortium.org**

