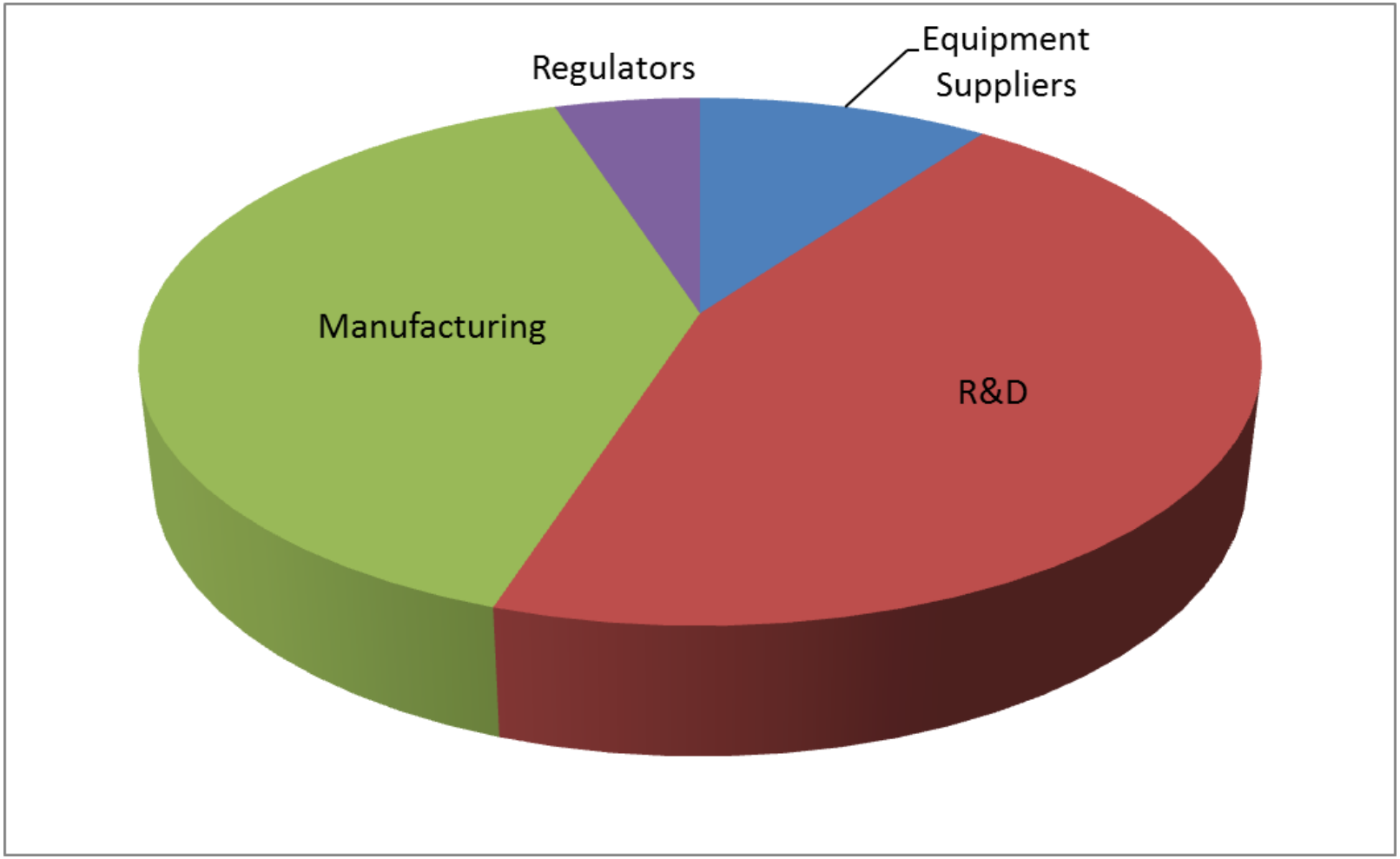
Topic 4: Needed Equipment and Associated Facility Cost
Group Demographics (1)



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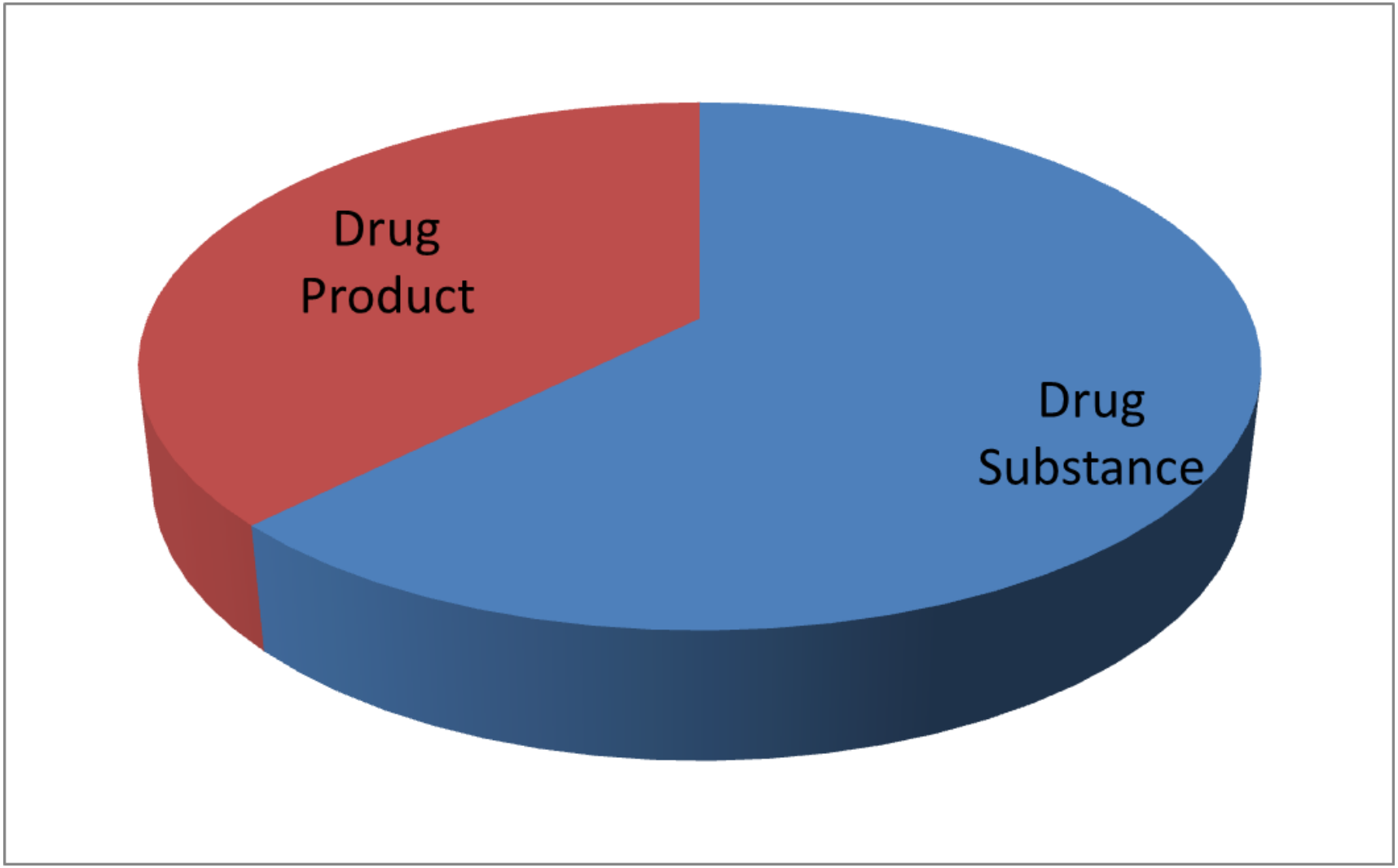
Group Demographics (2)



Statement 1

Recent investments in CP technology will spawn **iterative, innovation and prototyping of next generation CP equipment**, for use in the development, manufacture and supply of pharmaceuticals to the market place.

Recent investments in CP technology **will define how pharmaceuticals are developed, manufactured, and supplied** to the market for the decade(s) to come.

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Emerging CP technologies **will be installed into or as part of existing bricks-and-mortar pharmaceutical manufacturing facilities**

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Topic 4: Needed Equipment and Associated Facility Cost

What are the perceived technical challenges / barriers for introducing new equipment?

- For new equipment, operational knowledge is often missing
  - Gaps will be filled over time with conferences and publications
  - Opportunity for collaboration between academia, industry and equipment provider
  - This relationship worked really well for PAT equipment
  - Appropriate scale down/up models of equipment

- Drug substance
  - Adapting PFRs to allow for heterogeneous reactions
  - Materials of construction
  - Continuous isolation and drying equipment
  - Quantitative charging of solids to equipment to remove need for solution make-ups

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What are the perceived technical challenges / barriers for introducing new equipment?

- Drug Product
  - Design of excipients that aid flow (because APIs always flow well)
  - Mass feeders for the lower composition blend excipients
  - Containment, especially around feeding
  - Incorporation of ingredients for coating solutions
  - Relaxation period post tableting
- Analytical
  - Simple miniature sensors that behave and cost like thermocouples
  - Analysis for real-time content uniformity
  - Real-time chromatography
  - What do we do with all the data?
  - Be diligent with placement and selection of sensors – balance expensive sensors with other measurement methods

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What are the perceived operational challenges / barriers for introducing new equipment?

- Cleanability
  - Opportunities to better engineer equipment with smaller number of parts
  - Difference in approach between DP and DS
- Ensuring containment, particularly around product transfers
- Training of support staff from operators to first-line technical support
  - Worked well for equipment suppliers to help with training even after the FATs
  - Perhaps even more exaggerated with CMOs
- Overcoming the activation barriers with all first-time introductions

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What are the perceived facility challenges / barriers for introducing new equipment?

- Integration into the existing plant systems from Quality to Control
- Retrofit into existing brick and mortar structures
- Justifying the business case
- Unseating the batch king. Explaining that these are not like-for-like replacements, continuous equipment allows additional flexibility

Back up

Conference Program for the 2016 FDA-AIChE Workshop on Adopting Continuous Manufacturing

The Opportunity

Continuous processing has the potential to make the production of pharmaceuticals more responsive to patient needs. This workshop will address regulatory and other challenges associated with the implementation of this technology in pharmaceutical development and manufacturing. New technology conception to full incorporation has often required 20 + years. In some instances, uptake of technologies is never fully realized. Continuous manufacturing is the latest "initiative" that has met resistance to full-scale implementation despite the fact that many pharma companies used continuous manufacturing in the 1970's and 1980's for large-volume antibiotic and animal health products.

The Approach

This workshop addresses the issues surrounding full adoption of continuous manufacturing in pharmaceutical processing. Business cases for successful implementation will be shared, and focus groups will discuss these cases while addressing the top perceived issues. Technical sessions demonstrating the process and quality control benefits of implemented continuous manufacturing will be shared. The output of the workshop is targeted to inform ongoing regulatory guidance writing efforts.

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Moderators: Dan Blackwood and Derek Berglund

- Folks will be able to post questions to our session ahead of time
- Dan and Derek to introduce ourselves
- Do we need a disclaimer? I assume to absolve everyone that they speak for themselves and not for their companies? AGREED
- Introduce goals of our session
  - be good stewards to encourage adoption of continuous processing technologies
  - Seek opportunities for pre-competitive co-design (Vendors, Pharma, Generics, Academics, etc) and commercialize CP equipment DS and 2nd generation DP
  - potential list of eqpt suppliers we should investigate NEEDs WORK

DO NOT PRESENT THIS SLIDE

Topic 4: Needed Equipment and Associated Facility Cost

Moderators: Dan Blackwood and Derek Berglund

Themes (4)

- What are the perceived benefits of equipment or facility standardization?

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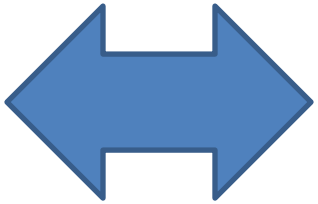
Themes (4)

- Are their benefits to standardizing equipment across the industry?
  - Would this reduce a PAI risk?
  - DP/DS?
  - Does this limit the eqpt to diversification in use?
  - What happens to vendor's IP position
  - How to encourage standardization? Push to ISPE/iQ/other symposia? Volunteers?
  - How can this be done without stifling innovation?
  - Opportunities for software standardization
- How to incentivize equipment manufacturers to develop prototype and then commercialize continuous equipment?
  - DP/DS/analytical
  - Can we garner any information from other industries on how to prototype and then pilot new equipment platforms?
  - What is the current state of equipment vendors? Do we have a comprehensive list?

Introduce 3 Provocative Statements

Recent investments in CP technology will define how pharmaceuticals are developed, manufactured, and supplied to the market for the decade(s) to come.



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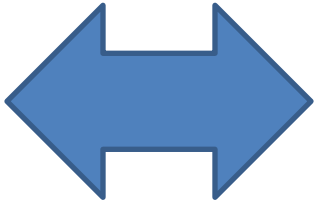
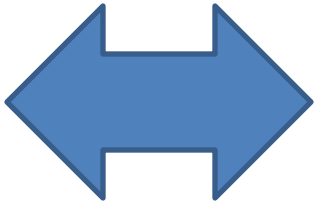


Emerging CP technologies will radically and disruptively influence the design of pharmaceutical manufacturing facilities

The creation of CP platform technologies will drive the efficient adoption of CP paradigms into the pharmaceutical industry



The efficient adoption of CP paradigms into the pharmaceutical industry will constantly evolve through incremental and disruptive innovative of CP equipment design evolutions

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Themes (1)

- What are the perceived technical challenges / barriers for introducing new equipment?
  - What is the largest need with respect to equipment?
    - Drug product / substance and analytical?
    - What is the current state of that equipment platform (prototype vs commercial ready)?
  - What unit operations are “shop-floor” ready for high performance operation
  - Equipment design for an uncertain future
  - What unit operations DP/API need additional design work
    - API: Reaction, Crystalization, Filtration, Drying, Milling
    - DP: Feeding, Powder Mixing, Granulation, Compression, Film Coating

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Themes (2)

- What are the perceived <u>operational</u> challenges / barriers for introducing new equipment?
  - Resource and time requirements for completion of IQ/OQ/PQ activities
  - Training of workforce
  - Integrated CP equipment vs De-couple Batch processing equipment
    - Cleaning and Rapid change-over of a CP facility
    - Equipment Reliability to ensure high OEE
  - Implementation of Low Cost/Low Maintenance/High Impact advanced sensors
  - Complexity: doesn't fit with typical operations paradigm
  - How to integrate into existing systems? Cleaning? Space? Automation?

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Themes (3)

- What are the perceived facility challenges / barriers for introducing new equipment?
  - Retrofit of existing facility to accommodate new integrated process equipment.
  - Coupling of material dispensing activities with material transformation/processing activities
  - Space requirements of CP equipment (e.g. headroom)
  - Facility design for an uncertain future?

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