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Overcoming Roadblocks to Innovation in Advanced Pharmaceutical Manufacturing

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Innovations in Pharmaceutical Manufacturing on the Horizon: A Virtual Dissemination Workshop
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Message

- Continuous Direct Compression is our best established success case study in advanced manufacturing
  - How did it happen?
  - Can we replicate it?
  - What are the roadblocks?
- Enabling widespread adoption as a catalyst for broader success

CDC is a clear success in innovation

- Multiple FDA approvals
- >60% of ongoing development efforts in OSD CM (personal communication from equipment companies)
- Dozens of ongoing projects at > 20 companies
- At least six suppliers of integrated lines (GEA, Glatt, Bohle, Fette, Powrex, Bosch)
- Moving beyond brand-based pharma and into OTC, generics
- Lines available at multiple universities and at CMOs
- CDC graduated from FDA ETT

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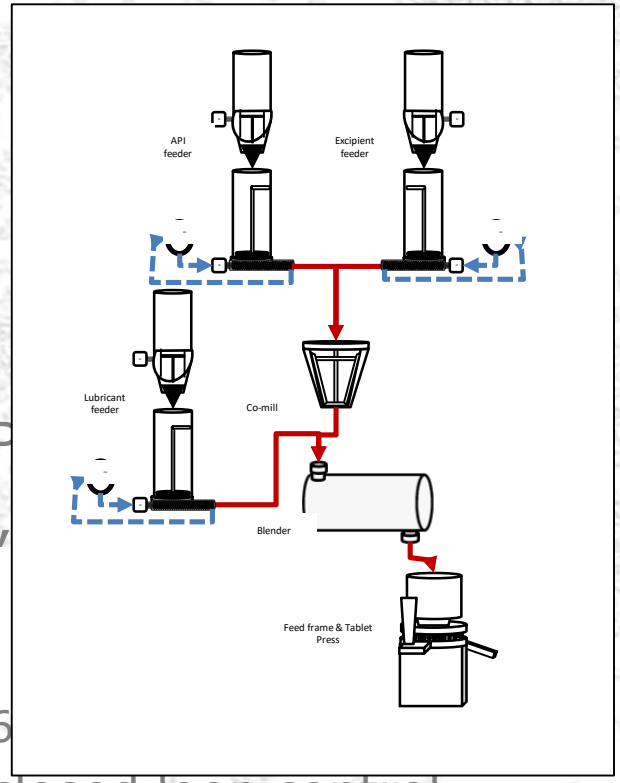

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- Multiple companies invest at Rutgers and elsewhere to expand case study library
- FDA provides funding to create knowledge base for CDC (~ $13M in 2016-2021)

Many things went right

- Academics were aware of the problem that needed to be solved: quality issues due to batch blending
- FDA provided early statement of regulatory support and also consistent commitment
- Funding was available throughout the technology life cycle
  - Early conceptual development (technology POC)
  - Commercial scale implementation
  - Extensive technology demonstrations
  - Early adopters

Roadblocks to replicating CDC success

- Lack of shared awareness of manufacturing problems that need to be solved
  - Technology dialogue between industry, agency, and academia is limited to a few forums and a small number of senior academics
- Regulatory uncertainty, mainly regarding harmonization and alignment
- Lack of early funding for new manufacturing technology POC
  - There is no established funding source for pharmaceutical manufacturing technology POC
- Valley of Death
  - Process from concept to commercial technology takes > 10 years and many $M
- Large upfront cost and long lead time for implementation
  - A single CM GMP line can cost >$20M
  - Lead time to line implementation ~ 3y
  - Including process development and regulatory approval, lead time> 5y
  - Too expensive and too long for most companies in the space, delays adoption, hinders momentum, creates adverse perception

Catalyzing success in APM

1. Build on CDC success to create momentum:
   a. Enable widespread implementation of CDC
      i. Create technology transfer laboratories that lower upfront cost and lead time for process implementation
      ii. Enable rapid approvals based on 100% inspection capabilities
      iii. Create platform formulations and processes
      iv. Facilitate process transfers between similar lines
2. Create pathfinder programs
   a. Identify manufacturing problems that need technology solutions,
   b. Provide seed funding for technology POC
   c. Engage more industry and more academics
3. Fund technology demonstration and commercialization (crossing the valley of death)
4. Fund technology implementation toolboxes (widespread adoption)
   a. Established knowledge
   b. Material property database
   c. Equipment performance database
   d. Technology standards (e.g., sensors)
   e. Modeling libraries and digital design tools
   f. Process control methods