Advanced Pharmaceutical Manufacturing:
A Perspective from the NSF Engineering Directorate

Pramod P. Khargonekar
Assistant Director for Engineering
National Science Foundation
NSF ENG

Investing in engineering research and education and fostering innovations to benefit society
ENG Initiatives and Priorities Address National Interests

- Innovations at the Nexus of Food, Energy, and Water Systems
- Risk and Resilience
- Urban Science
- Clean Energy Technology*
- Cyber-Enabled Materials, Manufacturing, and Smart Systems
  - Advanced Manufacturing*
- National Nanotechnology Initiative*
- Communications and Cyberinfrastructure
- Optics and Photonics
- Understanding the Brain
- Education and Broadening Participation
  - Inclusion across the Nation of Communities of Learners that have been Underrepresented for Diversity in Engineering and Science
- Innovation Corps

* National Initiatives
“Advanced manufacturing is a family of activities that
(a) depend on the use and coordination of information,
automation, computation, software, sensing, and networking, and/or
(b) make use of cutting edge materials and emerging
capabilities enabled by the physical and biological
sciences, for example nanotechnology, chemistry, and
biology.
It involves both new ways to manufacture existing products, and the
manufacture of new products emerging from new advanced
technologies.”

President’s Council of Advisors on Science and Technology
Report to the President on Ensuring American Leadership in Advanced Manufacturing
Key US Government Agencies in AM

• Department of Commerce (NIST)
• Department of Energy
• Department of Defense
• National Science Foundation
• NASA
• Department of Agriculture
  And many others
C-SOPS – An NSF ERC

- ERC – Interdisciplinary research and education using engineered systems approach
- Model university-industry-government partnership program
- C-SOPS Established in 2006
- Total NSF investment to-date: $33M
- Total expected from all sources: $100M
- C-SOPS Vision:
  “to be the national focal point for science-based development of structured organic particle-based products and their manufacturing processes”
C-SOPS – Goals

• To understand the impact of material properties and processing inputs on product structure and performance and
• To use this understanding to design, control, and optimize products and their associated manufacturing processes.
• C-SOPS has made very significant progress towards these goals and is poised for major contributions to continuous pharmaceuticals manufacturing
C-SOPS – Goals

• To understand the impact of material properties and processing inputs on product structure and performance and
• To use this understanding to design, control, and optimize products and their associated manufacturing processes.
• C-SOPS has made very significant progress towards these goals and is poised for major contributions to continuous pharmaceuticals manufacturing
C-SOPS Areas of Excellence

• **Material characterization methods:**
  - powder flow and cohesion, powder hydrophobicity, powder electrostatics, online measurements of powder composition and density, effects of shear on material properties, and many others

• **Innovative processes and products:**
  - continuous manufacturing, nanotechnology-enhanced bioavailability, thin films, dry impregnation, microfluidics-based microdosing, pharmaceutical nanosuspensions

• **Process modeling**
  - (FEM, DEM, Pop. Balances, flowsheet modeling, statistically-based models)

• **University-industry-academic partnership**
The use of biological systems comprised of biomolecules, cells and biomaterials, or the products of biological systems, to generate new devices and constructs with a view towards scalability and industrialization

**Vision:** To combine advances in biology with innovative design to engineer the next generation of biologically inspired products

Production of liposomal pharmaceuticals in a microfluidic system

Fabrication of complex, biologically active, three-dimensional constructs
Cellular Biomanufacturing DCL

Significance

• Cell-based therapies and diagnostics have the potential to revolutionize human healthcare
• Processes with cells as products present major engineering challenges; new therapies and cell-based products depend critically on robust and reliable biomanufacturing technology

NSF seeks to support fundamental research on:

• Novel cell expansion, differentiation, characterization, monitoring, separation methodologies
• Reproducible, reliable cellular biomanufacturing processes

NSF 15-065
Related Core Programs

• Division of Chemical, Biological, Environmental and Transport Systems
• Process and Reaction Engineering
• Chemical and Biological Separations
• Particulate and Multiphase Processes
Center for Pharmaceutical Processing Research – An NSF I/UCRC

• CPPR - Established in 1995
• Collaboration between Purdue University, University of Connecticut, the University of Puerto Rico, and the University of Minnesota
• Industry Partners: AbbVie, AstraZeneca, Biogen Idec, Eli Lilly, Genentech, GlaxoSmithKline, Medimmune, Regeneron, SP Scientific
CPPR Research

• Interplay between **physical and mechanical properties** of pharmaceutical materials and **processing conditions** and critical **quality attributes** of the resulting product.

• Exploration, development and refinement of new technologies for **process monitoring and control**, leading to improved product quality based on process understanding.

• **Technical areas:** granulation, powder blending, PAT, pharmaceutical applications of supercritical fluid technology, freeze-drying, nucleation and crystal growth processes, filtration, sterilization of disperse systems, and microparticulate technology.
Center for Pharmaceutical Development – An NSF I/UCRC

- CPD - Established 2010
- Collaboration between Georgia Tech, University of Kentucky, University of Kansas and Duquesne University
- Industry Partners: AbbVie, Alkermes, Allergan, DSM Innovative Synthesis, Genentech
CPD Research

- **Manufacturing**: Novel and improved routes to small-molecule targets via biocatalysts and integration of reaction and product/(bio)catalyst separation.

- **Formulation**: Predict the long-term stability of the active ingredient in vials, tablets and vaccines to extend the safety of drugs and vaccines.

- **Analytical**: Establish accelerated and non-accelerated stability testing of pharmaceutical products to enhance the shelf-life of pharmaceutical products and to explore rapid identification of drug product to detect counterfeit, degraded and adulterated drugs.
Fostering Innovation in Pharmaceutical Manufacturing

• Pharmaceutical Manufacturing: new topic in NSF SBIR program
• Intended Broader Impacts:
  – Improve the efficiency, competitiveness and output of the pharmaceutical manufacturing sector;
  – Reduce cost, risk and time-to-market of new drugs and biological products;
  – Increase the net preservation of natural resources;
  – Reduce the use of toxic constituents and extreme conditions, and waste production; and
  – Address major market opportunities in the developing world.
Covaris Inc - Continuous Manufacturing of Nanoparticle Drugs Using Focused Acoustics

**Broader Impact:** Enable continuous manufacture of drug nanoparticles by controlling nanocrystallization using a novel focused acoustical field.

**Intellectual Merit:** Focused acoustics have the advantage of delivering highly efficient, controllable, scalable energy field to the crystallization zone.

**SBIR Award 1448429**
CONTINUUS - Multistep Continuous Process to Overcome Limitations of Batch Manufacturing

- **CONTINUUS Pharmaceuticals** – a spin-out company of a collaboration between MIT and Novartis on continuous manufacturing.

- **Broader Impact:**
  Enable the commercial development of an integrated continuous pharmaceutical manufacturing system.

- **Intellectual Merit:**
  Further develop novel process technologies - a membrane separator, a rotary filter and a drum dryer.

- SBIR Award 1447944
Conclusions

• NSF Engineering has a strong interest in advancing manufacturing research and innovation.
• NSF strongly supports university-industry-academic partnerships.