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The National Institute for Pharmaceutical Technology & Education

Advanced Manufacturing Technologies: Accelerating Injectable Product Development and Addressing Drug Shortages

Sponsored by NSF

January 9-11, 2024

Texas A&M Bush School of Government & Public Service, 1620 L Street NW, Washington, DC

FINAL DRAFT

EXECUTIVE SUMMARY

The drug discovery, development, and regulatory approval process typically takes up to 15 years. This lengthy time frame makes it hard to respond to emergencies requiring new therapies, deprives patients of fast access to life-saving medicines, decreases the profitability period of pharmaceutical companies, and contributes to the high cost of new medicines. Moreover, the COVID-19 pandemic has made the need for faster drug development and regulatory evaluation process clear.

To address this critical issue of national importance, we propose to organize a Pathfinding Workshop focused on two major goals:

1. To identify scientific, technological, and regulatory mechanisms capable of reducing injectable drug product development time frame without increasing patient risk, and
2. To integrate these mechanisms into a coherent strategy for accelerating the discovery, development, and regulatory approval process of these important drug products.

The proposed workshop will bring together a focused group of thought leaders from academia, industry, and regulatory agencies, to discuss the critical elements needed to accelerate drug development, and regulatory evaluation based on recent scientific and technical advances in medicine, biology, chemistry, materials science, biostatistics, and advanced manufacturing technologies. These discussions will be led by pre-selected panelists with an established track record in their respective fields. Acceleration mechanisms will be examined from multiple perspectives, including the strength of the underlying science, technical feasibility, and regulatory acceptability. Brainstorming and analysis with the participation of experts across the relevant disciplines will enable significant outcomes, which wouldn't be achieved in any existing scientific communication forum or conferences.

Acceleration mechanisms deemed to be potentially effective will be selected for further analysis by a focused multidisciplinary team of workshop participants. Workshop participants will be tasked with integrating these mechanisms into a strategic plan and developing an implementation pathway. These documents, which will be the main output of the workshop, will serve as a blueprint for the Federal Government, industry, and academia to direct efforts in this field.

PROBLEM STATEMENT

The drug discovery, development, and regulatory evaluation process, from the point where a molecule is identified as a potential therapeutic agent, to the point where it is approved for commercialization as a drug product, can take up to 15 years. This lengthy process involves many stages, including the determination of efficacy, safety, toxicity, and therapeutic regime, identification of target populations, side effects, and interactions, selection of a feasible synthetic pathway, and development of a product formulation and a reliable manufacturing process.

Every step of this process is informed by science but it is also heavily laden with legacy practices. Industry and regulatory agencies are appropriately conservative and risk-averse. However, in recent years, many approaches have emerged that are capable of accelerating the discovery, development, and regulatory evaluation process while preserving patient safety. These include bioassays that can determine tissue toxicity and tissue targeting; models that can predict individual absorption, distribution, metabolism, elimination, and toxicity; prediction of clinical response in diverse patient populations based on sub-clinical exposure: chemistry, manufacturing, and control strategies that can accelerate development; and advanced manufacturing methods that greatly accelerate product and manufacturing process development. In combination, these and other emerging approaches can substantially accelerate the preclinical and clinical development stages, and can also facilitate rapid and reliable regulatory evaluation.

These approaches are emerging in various disciplines and have not been integrated as part of an overall strategy for accelerating drug product development and regulatory evaluations.

This Pathfinder Workshop will achieve two goals:

Goal 1: To identify Scientific, Technological, and Regulatory barriers that prevent significant reductions in the development time and efficient, reliable manufacturing for injectable drug products.

Goal 2: To identify mechanisms capable of significantly reducing the time required for drug development, and improving the efficiency of manufacturing for more consistent quality, and integrate these into a coherent strategy and implementation plan for reduced risks to patients.

Benefits of Participating in the Workshop

The Workshop Steering Committee will use the material generated during the workshop to create a coherent Strategy and Implementation plan for accelerating Drug Development and Regulatory Approval of injectable products. This document will be the main tangible output from the workshop. The workshop will lead to the creation of a blueprint for accelerating injectable drug development and regulatory evaluation that will be enormously valuable in guiding the selection of research activities by academics, resource allocation by federal agencies, and selection of strategies by Industry. The multidisciplinary discussions to be conducted before, during, and after the proposed workshop will synergize currently isolated efforts by workshop participants, potentially leading to the identification of opportunities for collaboration.

Workshop Agenda – January 9, 2024:

8:00 - 8:30 Registration and Breakfast

8:30 – 8:50 Introductions and Review of goals, roles, and expectations, **Vadim Gurvich, NIPTE**

8:50 – 9:25 PLENARY TALK: Scientific Challenges in the Development of Complex Injectables
Robert Lionberger, Director, Office of Research and Standards, Office of Generic Drugs, FDA

9:25 - 10:00 PLENARY TALK: The Race to End Drug Shortages through Partnership & Patient-Centric Design
Laura Bray, Founder, Angels for Change

10:00 – 10:15 Break

10:15 – 12:15 SESSION 1: Patient-centric discussion on injectable drug products
(**Moderator: Robin Bogner, University of Connecticut/NIPTE**)

- 10:15 – 10:35 Presentation of issues: Identify scientific, technological, and regulatory issues that need to be resolved, **Parag Kolhe, Pfizer**
- 10:35 – 10:55 Panel Discussion
Glenn Wright, PDA; Hailing Zhang, FDA; Pieter Muntendam, SQ Innovation
- 10:55 – 11:25 Small group discussions: Breakthrough strategies for overcoming barriers
- 11:25 - 11:35 Break
- 11:35 – 11:55 Reports by small groups
- 11:55– 12:15 Open forum discussion

12:15 – 1:15 Lunch

1:15 – 3:15 SESSION 2: Injectable drug device combinations **(Moderator: Eric Munson, Purdue/NIPTE)**

- 1:15 – 1:35 Session Chair presentation: **Manuel Sanchez-Felix, Halozyme Therapeutics**

  State-of-the-art in injectable device drug combinations, development and evaluation including methods to accelerate.

  Barriers to accelerating combination product development and evaluation.

  Main opportunities for accelerating product development and evaluation.
- 1:35 – 1:55 Panel Discussions
Manuel Sanchez-Felix, Halozyme Therapeutics; Galen Shi, Lilly; Eric Munson, Purdue/NIPTE
- 1:55 – 2:25 Breakout groups (by barrier): Breakthrough strategies for overcoming barriers
- 2:25 – 2:35 Break
- 2:35 – 2:55 Reports by breakout groups
- 2:55 – 3:15 Open forum discussion
- 3:15 – 3:30 Break

3:30 – 5:30 SESSION 3: Injectables with Complex Formulations and Assessment (**Moderator: Xiuling Lu, University of Connecticut/NIPTE**)

- 3:30 – 3:50 Summary presentation: **Annette Bak, AstraZeneca and Robert Lionberger, FDA**
  - State-of-the-art formulation development for complex injectables and their quality evaluations.
  - Barriers to accelerating Product Formulation and Process Development.
- 3:50 – 4:10 Panel Discussions (**Yan Wang, Annette Bak, Xiuling Lu**)
- 4:10 – 4:40 Small group discussions: Breakthrough strategies for overcoming barriers
- 4:40 – 4:50 Break
- 4:50 – 5:10 Reports by small groups
- 5:10 – 5:30 Open forum discussion

5:30 – 6:15 Cocktail hour and Poster Session

6:15 - 7:30 Reception

Workshop Agenda – January 10, 2024:

7:45 - 8:15 Registration and Breakfast

8:15 – 8:30 Day 1 recap, **Fernando Muzzio, Rutgers University/NIPTE**

- Short presentations from attendees based on Section 1, 2 and 3 outcomes

8:30 - 9:00 Keynote 1 Continuous manufacturing of complex Injectables, PAT and AI **Antony Costa, DIANT Pharma**

9:00 – 9:30 Keynote 2: Advancing Freeze Drying through Technical Innovation: A Review of Current Efforts, **Emily Gong, PSI**

9:30 – 9:45 Q&A (**Diane Burgess** and **Robin Bogner**, **University of Connecticut/NIPTE**)

9:45 – 10:00 Break

10:00 – 12:00 SESSION 4: Advanced manufacturing in injectable products (**Moderator: Diane Burgess**)

- 10:00 – 10:20 Session Chair presentation: (To Be Announced)
  - Main opportunities for Product Formulation and Manufacturing Process: AI-based prediction, advanced/continuous manufacturing, in-line controlling systems, scale-up process, modular GMP operations, etc.
  - Presentation by a large-scale manufacturer (To be Announced)
  - Presentation by a small-scale manufacturer (**Joe Bagan, 503B outsourcing facility**)
- 10:20 – 10:40 Panel Discussion
- 10:40 – 11:10 Small group discussions: Breakthrough strategies for overcoming barriers
- 11:10 – 11:20 Break

11:20 – 11:40 Reports by small groups

11:40 - 12:00 Open forum discussion

12:00 – 1:00 Lunch

1:00 – 3:00 SESSION 5: Advanced modeling and analytical tools
(Moderator: Bodhi Chaudhuri, University of Connecticut/NIPTE)

1:00 – 1:20 Session Chair presentation: (**Michael Tian, FDA** and **Yongchao Su, Merck**)

Main agency-based opportunities for accelerating evaluation. Breakthrough Therapy Designation, Emerging Technologies Team

1:20 – 1:40 Panel Discussions (**Yongchao Su, Merck; Francis Kwofie, GSK; Michael Tian FDA; Steven Castleberry, Genentech**)

1:40 – 2:10 Breakout groups (by barrier): Breakthrough strategies for overcoming given barriers

2:10 – 2:20 Break

2:20 – 2:40 Reports by breakout groups

2:40 – 3:10 Open forum discussion

3:10 – 3:30 Break

3:30 – 5:30 SESSION 6: Pathfinding – Small group breakouts, brainstorming, whiteboarding
(Moderator: Alina Alexeenko and Nate Milton Purdue University/NIPTE)

Workshop Agenda – January 11, 2024:

8:15 - 8:45 Registration and Breakfast

8:45 – 9:00 Day 2 recap **(Eric Munson, Purdue University/NIPTE)**

Short presentations from attendees based on Section 4-6 outcomes

9:00 - 9:30 Keynote 3: Addressing supply chain vulnerabilities with innovative solutions
Michael Levy, USP

9:30-10:00 Keynote 4: Innovation through Advanced Manufacturing: Learning from the Future
Xiaoming Xu, FDA

10:00-10:15 Break

10:15-12:15 SESSION 7: Policy and Regulatory Perspective
Moderator: Stephen Colvill, Duke Margolis Center for Health Policy)

10:15 – 10:55: Panel Discussions (Xiaoming Xu, FDA; Michael Levy, USP; Stephen Colvill - INVITED)

Regulatory barriers to accelerating Industry Product and Process Development

10:55 – 11:25 Small group discussions: Breakthrough strategies for overcoming barriers

11: 25- 11:35 Break

11:35 – 11:55 Reports by breakout groups

11:55 – 12:15 Selection of a Workshop Report Development Committee

12:15 - 1:00 Lunch

1:00 **WORKSHOP ADJOURNS** – Thank you! General Audience departure

CLOSED SESSION—

1:00 – 3:00 Organizing Committee - Development Committee Discussion & Report Session