Fostering innovation through OPQ's Emerging Technology Program

Presented by:

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Learning Objectives

- Describe OPQ's Emerging Technology Program (ETP)
- Describe landscape of emerging technologies in the ETP
- Describe a case study of how collaboration through the ETP can support the implementation of innovations

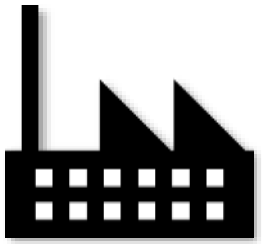
The Importance of Emerging Technologies

US FDA Center for Drug Evaluation and Research

Why are Emerging Technologies important for both FDA and pharmaceutical industry?

- **Addresses the underlying causes of drug shortages**
  - Helps mitigate or prevent future production problems

- **Improves manufacturing efficiency**
  - Increase process robustness
  - Lower manufacturing costs
  - Increase supply chain flexibility



- **Facilitates new complex generic products**
  - Novel analytical tools to characterize complex drug substances and products
  - Support establishment of pharmaceutical equivalence and/or bioequivalence
  - Improve the availability of complex generic products to the American public

Generic Industry and Emerging Technologies

- Emerging Technology can provide benefits to the generic drug industry
- CDER's Emerging Technology Team is working with generic industry
- There are challenges to implementation though:
  - Adoption of emerging technology requires new investment
  - Changing inventory of products being manufactured (platform technologies)
  - Development of new knowledge and skills

Through Collaboration can Overcome these Challenges and Foster Innovation

CDER Emerging Technology Program

US FDA Center for Drug Evaluation and Research

Mission

Encourage and support the adoption of **innovative technology**

to modernize pharmaceutical **development and manufacturing**

through **close collaboration** with industry and other relevant stakeholders

Team

A small **cross-functional** Emerging Technology Team (ETT)

with representation from all relevant FDA **quality assessment and inspection** programs

(CDER/OPQ, CDER/OC & ORA)

Program Objectives

To serve as a centralized location for external inquiries on novel technologies

To provide a forum for firms to engage in early dialogue with FDA to support innovation

To ensure consistency, continuity, and predictability in review and inspection

To engage international regulatory agencies to share learnings and approaches

To identify and evaluate potential roadblocks relating to existing guidance, policy, or practice

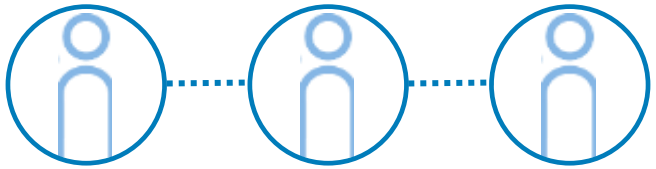
To facilitate knowledge transfer to relevant CDER and ORA review and inspection programs

To help establish scientific standards and policy, as needed

Contact us: CDER-ETT@fda.hhs.gov

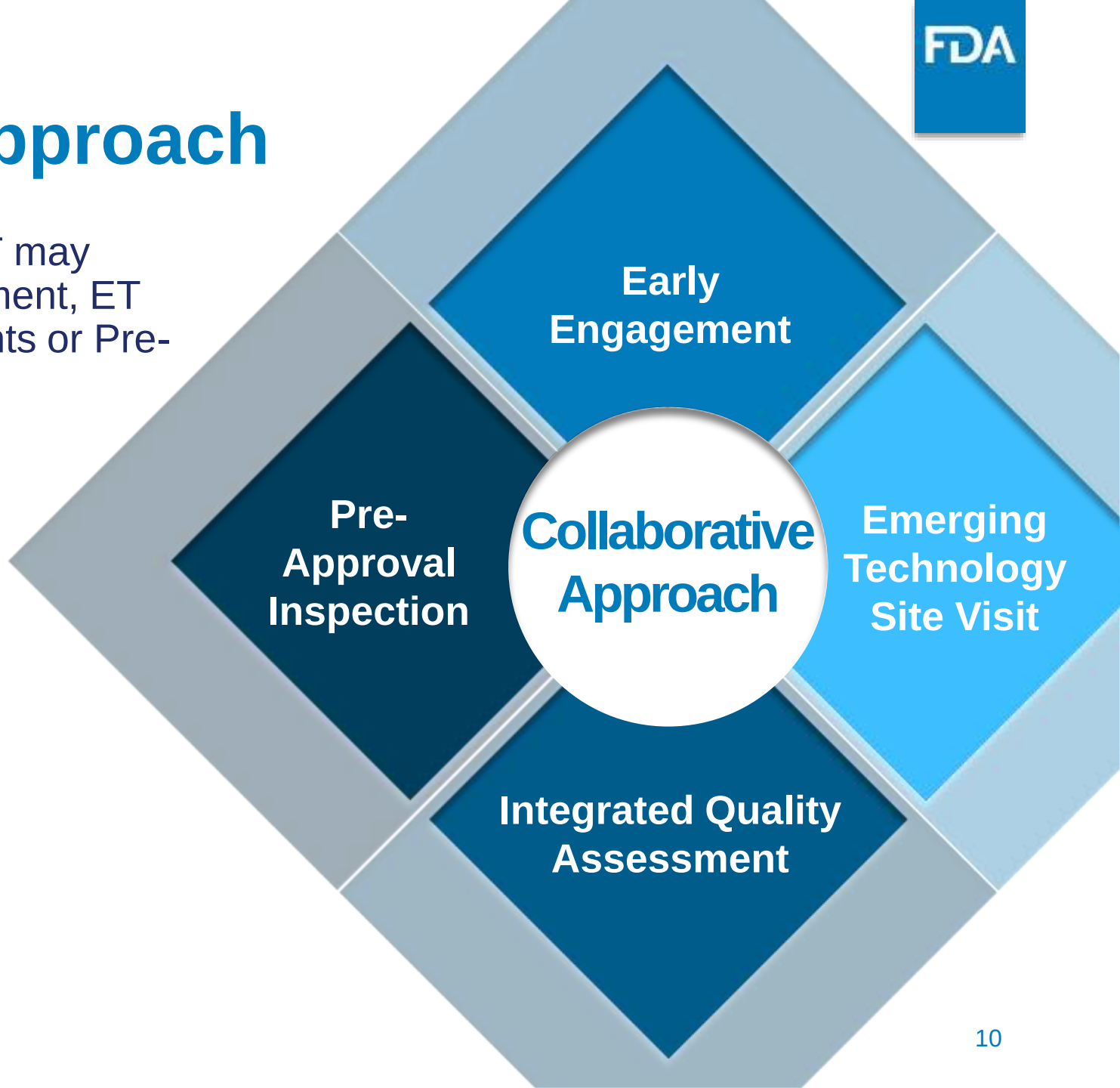
ETT Collaborative Approach

Over the course of an ETP project, ETT may employ a combination of early engagement, ET site visits, integrated quality assessments or Pre-Approval Inspections



The same ETT representative(s) will be involved in the entire process

The composition of a review team will likely remain the same throughout the entire process



For ETT Activities visit the ETP website:

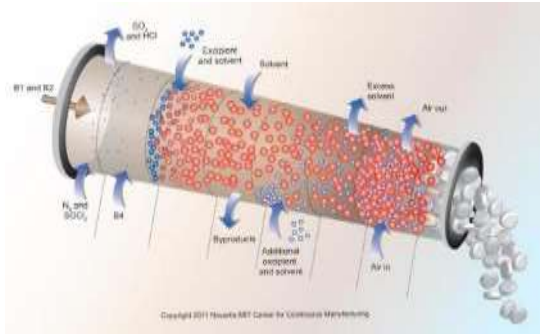
https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm523228.htm

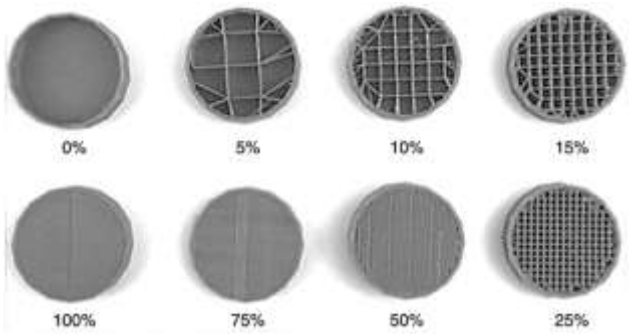
Examples of Emerging Technology

US FDA Center for Drug Evaluation and Research

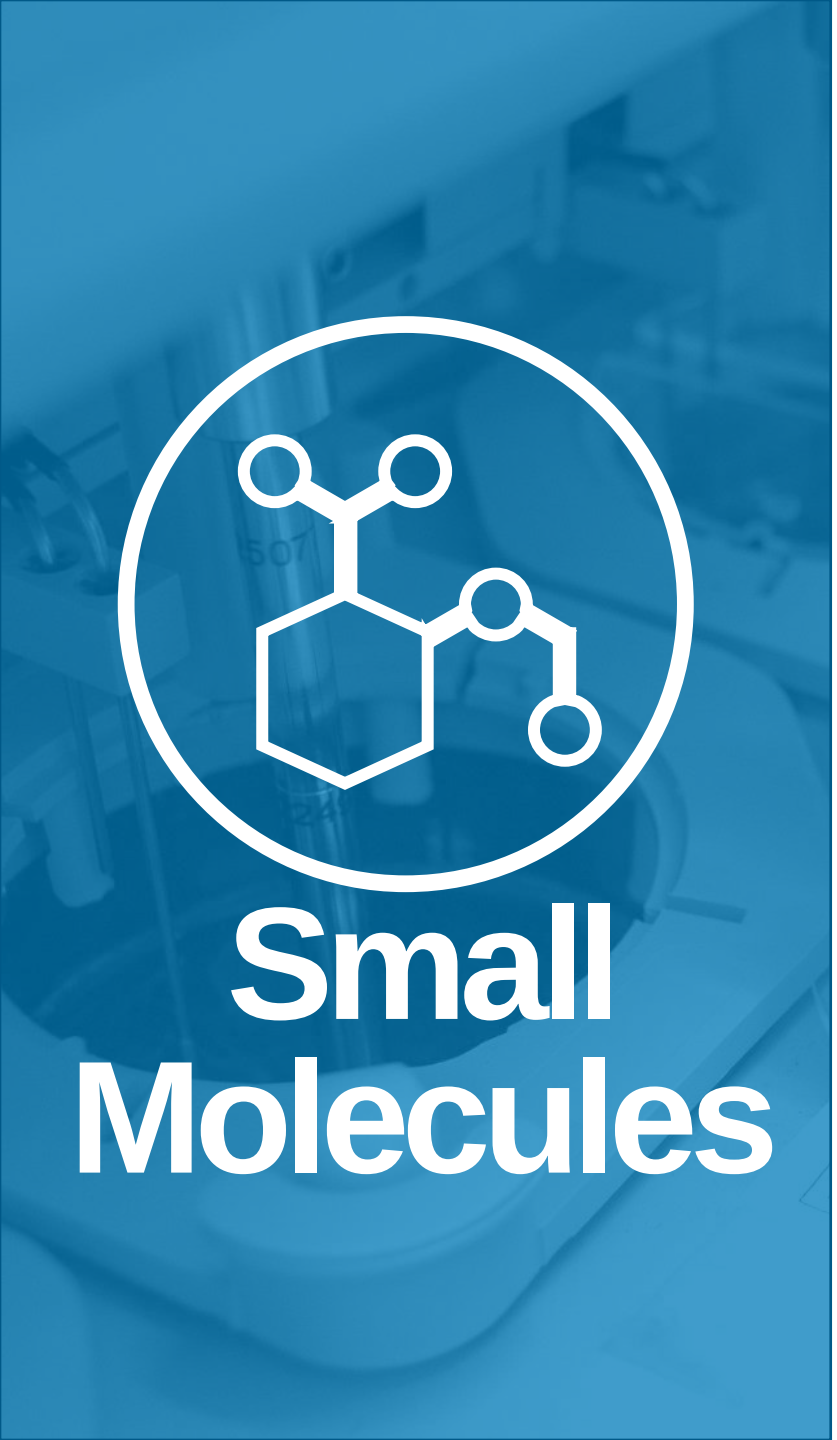
What are Emerging Technologies?

- Novel **manufacturing methods** to improve process robustness and efficiency
- Novel **dosage forms** or delivery systems to improve drug delivery and targeting
- Novel **analytical tools** to improve product quality testing, process monitoring and/or control





FDA has limited assessment experience due to its relative novelty and has an impact on product quality



FDA Experience: Emerging Technologies

- Continuous manufacturing of drug substance
- Continuous manufacturing of drug product
- End-to-end CM
- Pharmacy-on-demand
- Model-based control strategies
- Continuous aseptic spray drying
- 3D printing manufacturing
- Ultra long-acting oral formulation

Multiple Products

FDA Experience: Emerging Technologies

- Distributed Manufacturing
- Closed aseptic filling system
- Isolator and robotic arm for aseptic filling
- Novel container and closure system for injectable products
- Novel analytics

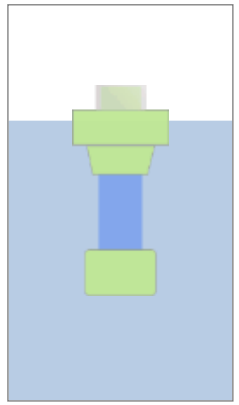
Case Study

US FDA Center for Drug Evaluation and Research

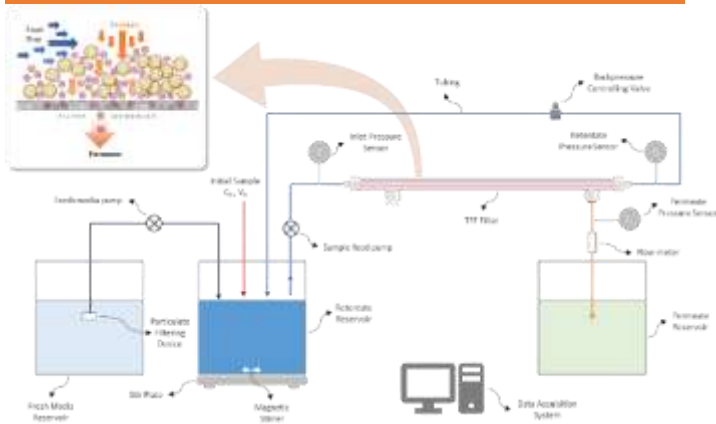
Case Study #1: Novel Analytical Tools

- In Vitro Release Test (IVRT)
  - Measure the in vitro rate and extent of drug release
  - Useful for: Product development, Quality control, and Bioequivalence
- Analysis of drug release from dispersed systems requires “separation of free drug”
- Common approach uses dialysis membrane
  - Challenges include method introduces rate-limiting step
  - Impact IVRT method’s discriminatory power

Dialysis

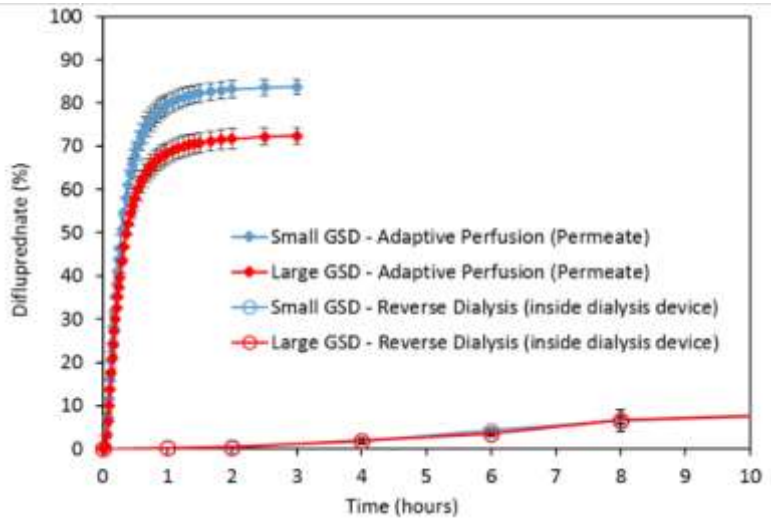


Adaptive Perfusion



Case Study #1: Novel Analytical Tools

- Adaptive perfusion is separation method based on the principle of tangential flow filtration (TFF)
- Achieve size-based separation of the particulates
- Simultaneous analysis of the released drug as well remaining drug
- Eliminate rate limiting step
- Potential to assess the impact of manufacturing process on performance of complex drug products.



Public Health Impact:
Improve the availability of complex generic products to the American public

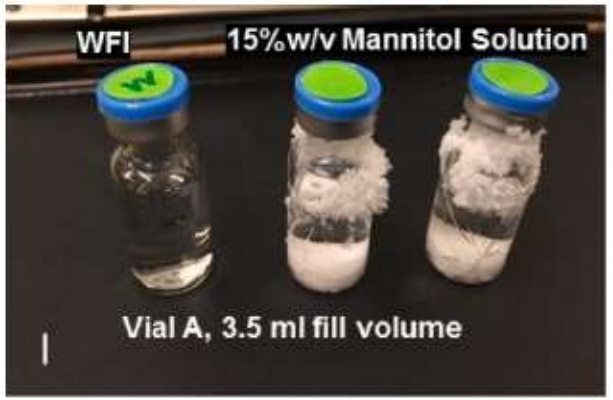
D. Patel, Y. Zhang, Y. Dong, H. Qu, D. Kozak, M. Ashraf, X. Xu. *Adaptive Perfusion: An In Vitro Release Test (IVRT) for Complex Drug Products.* Journal of Controlled Release (**2021**), 333, pp.65-75.

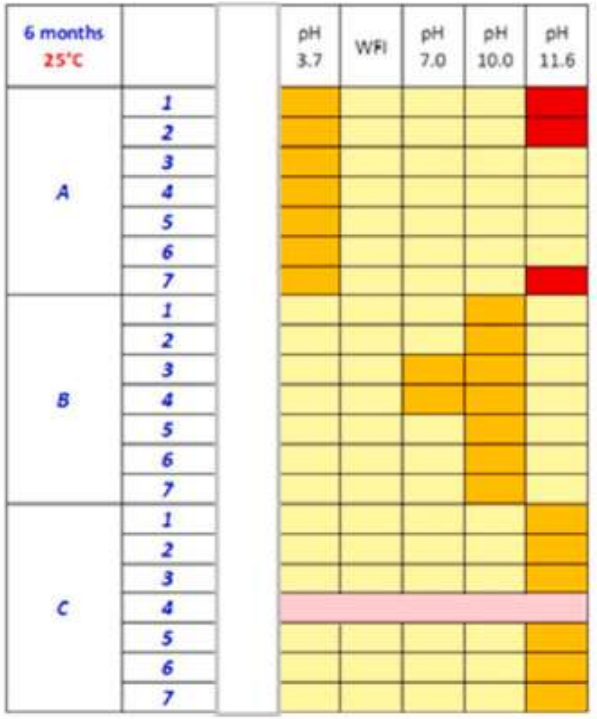
Case Study #2: Quality Attributes of CCS for Parenterals

- There have been recalls due to glass flakes, breakage, and/or particles observed in marketed formulations
  - E.g. epoetin alpha injection, sodium thiosulfate injection, and amikacin sulfate injection
- Borosilicate glass vials may undergo dissolution of glass network at high pH or at elevated temperatures
- Other common problems observed in glass containers are breakage, cracks, chipping, and particulate generation
- Generated during drug product manufacturing, transportation, or during administration

Case Study #2: Quality Attributes of CCS for Parenterals

- Innovative CCSs developed by suppliers accepted into the ETP
- FDA developed systematic platform testing approach capable of assessing common failure modes of pharmaceutical glass container closure systems
- Scientific approaches informed quality assessment of regulatory applications utilizing the novel CCSs
- Collaborated on filing strategy to speed adoption across product lines and manufacturing sites





Public Health Impact:
Increased supply of high-quality vials for injectable drug products and vaccines

Srinivasan C., *et. al.* Int. J. Pharma. 568 (2019) 118510
Ma, Y., *et. al*. Int. J. Pharma. (2021) 120248. https://doi.org/10.1016/j.ijpharm.2021.120248

Together we can overcome challenges and foster the implementation of innovations that improve product quality

Challenge Questions

- Is this statement true or false?

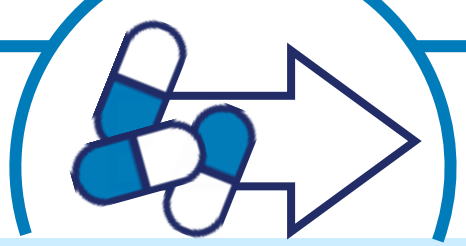
  "Emerging Technology can provide benefits to the generic drug industry"

- Is this statement true or false?

  "Collaborative interactions with the Emerging Technology Team can help navigate potential regulatory uncertainty when implementing novel technology"

Acknowledgements

Emerging Technology Team



OPQ Leadership

Industry Partners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