

# **The Emerging Technology Team: FDA's Tool To Promote Pharmaceutical Innovation and Modernization**

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## OVERVIEW

- ✓ Pharmaceutical Innovation: Introduction, Challenges and Promises
- ✓ FDA Initiative: The Emerging Technology Team (ETT)
- ✓ Publicly Known Emerging Technologies: Sample Case Studies
  - Continuous Manufacturing
  - 3-D Printing
  - Digital Medicine/Ingestible Sensor Technology

## What is Innovation or Emerging Technology?

People differ in their understanding of what innovation really means:

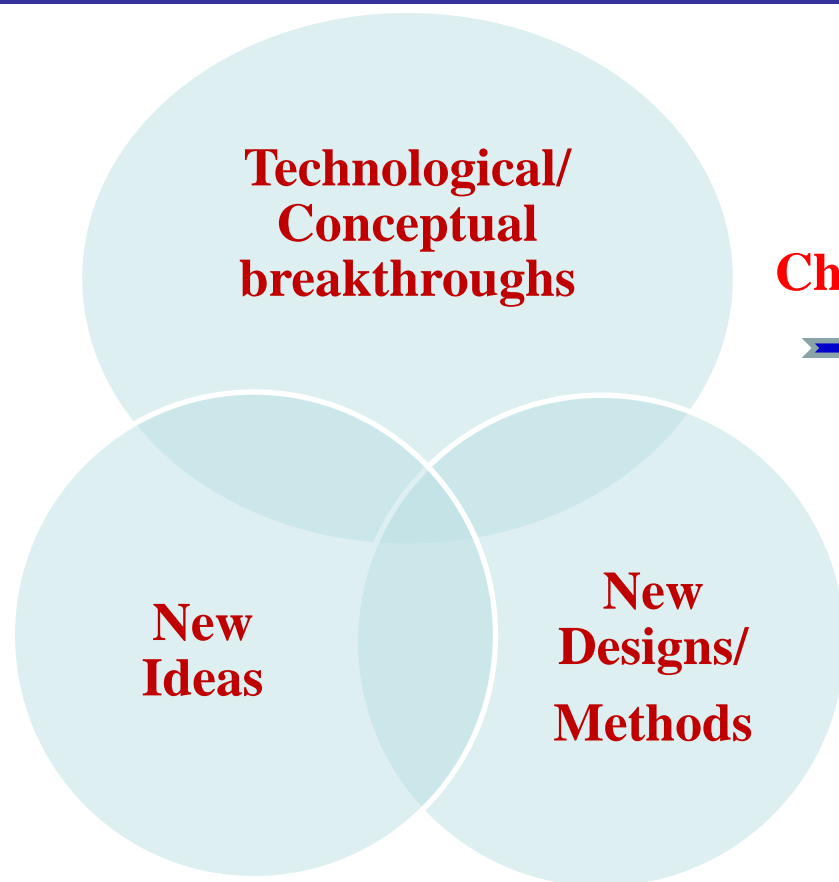


**"I want you to find a bold and innovative way  
to do everything exactly the same way  
it's been done for 25 years!"**

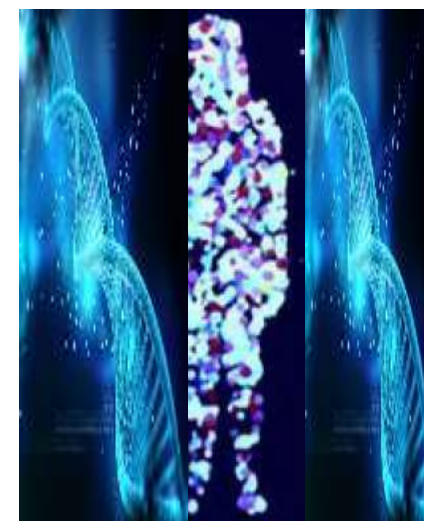
## What is Innovation?

- No single definition may suffice
- The introduction of something new: a new idea, method, or device for significant positive impact
- A process of applying novel discoveries, breakthrough ideas for solving problems
- Pharmaceutical innovation may be more narrowly defined

# Challenge: Viable Pharmaceutical Innovations



**Challenge of Viability**



**System/disease complexity**

**Innovation**

# “Translational Gap”: Challenges of Developing Viable Innovative Technologies

## Scientific Advances



*“Translational gap”*



Cost-Effective Novel  
Therapeutics



*“Translational gap”*



Traditional drug  
development, including  
manufacturing

Pharmaceutical Innovations  
Modernized development,  
including manufacturing

Need for collaborative  
exchange between academia,  
pharmaceutical industry and  
regulatory agencies

## Addressing the Translational Gap: The Regulatory Aspect

- Important structural role for science-based regulatory input for facilitating meaningful pharmaceutical innovation & modernization

**FDA Initiative: The  
Emerging Technology  
Team (ETT)**

## What is Emerging Technology (ET)?

- Broadly pertains to technology aimed towards pharmaceutical innovation and modernization, with a promise for significant impact on product quality and/or patient outcome
- By definition, ET will generally be unfamiliar, in both industrial and regulatory contexts, hence with limited or no regulatory precedence



## Emerging Technology: Scope

May Pertain to Any Aspect of Drug Development

- Innovative early pharmaceutical development
- Novel dosage formulations
- Innovative or modernized manufacturing/ manufacturing design (e.g., scale-up and commercialization)

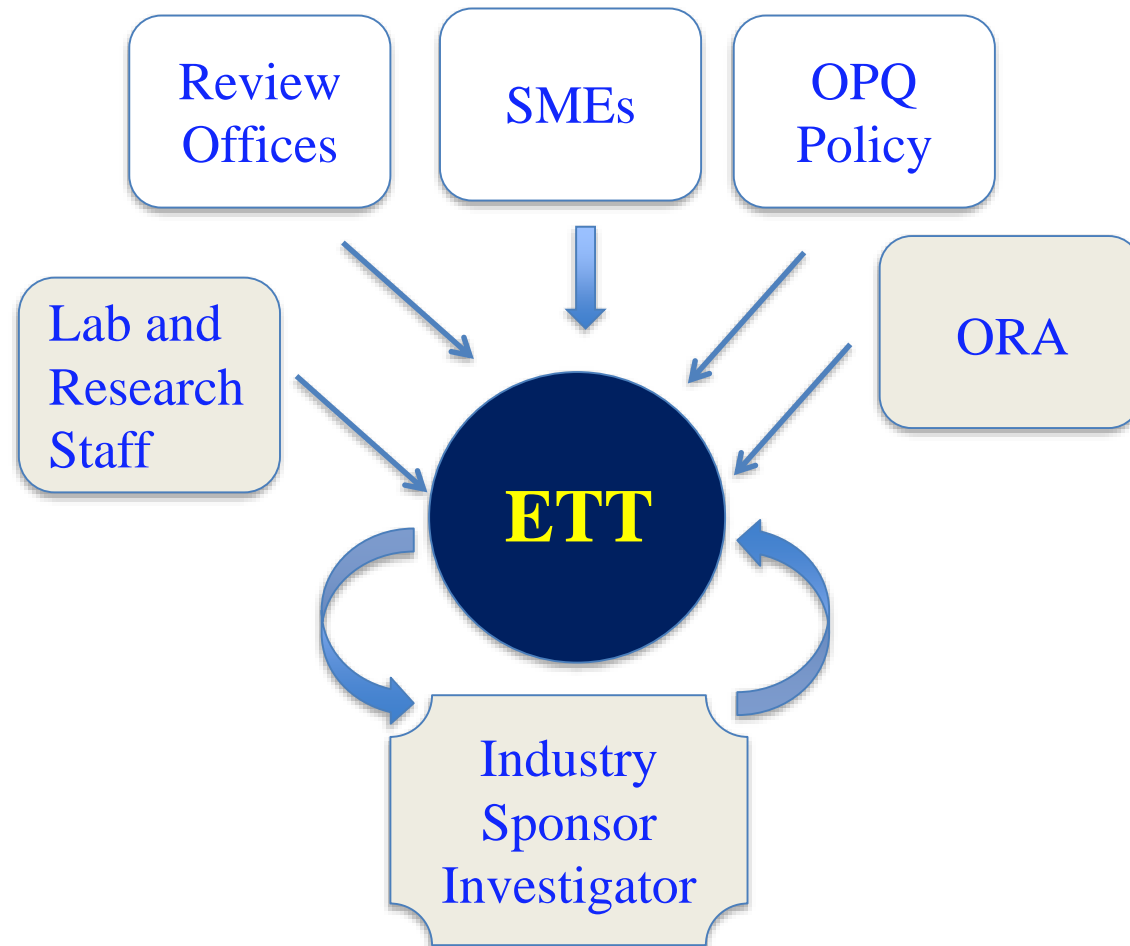
## Emerging Technology: Scope (Contd)

- Quality control testing technology
- Novel container closure systems
- Innovative drug designing
- Targeted drug delivery
- Novel molecular therapeutics

## Examples of Emerging Technology

- Continuous manufacturing of drug substances and drug products
- Use of robots in pharmaceutical manufacturing
- 3-D Printing (3-D bio-printing)
- Novel container and closure systems for injectable products
- Digital medicine/ingestible sensor technology

# FDA Initiative: Emerging Technology Team (ETT)



A cross-functional team, with representation from all relevant FDA CDER review and inspection programs, including OPQ and ORA

## Emerging Technology Team (ETT)

- Serves as a centralized point-of-contact for emerging technology inquiries/proposals from sponsors/applicants
- Provides a centralized collaborative platform for FDA and industry to accelerate the development and adoption of emerging technologies
- Operates on the principle of rigorous science-based assessment of innovative technologies while balancing risk vs. benefit

# Emerging Technology (ET) Draft Guidance

## Advancement of Emerging Technology Applications to Modernize the Pharmaceutical Manufacturing Base Guidance for Industry

### *DRAFT GUIDANCE*

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <http://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Sau L. Lee 240-506-9136.

U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)

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Pharmaceutical Quality/CMC

Augments the existing  
regulatory procedures by  
providing science-based  
consultations, guidance  
and /or regulatory  
recommendations  
concerning ET

## Early Stage Development-Related Consultation

### When:

- You have the option to seek agency perspective regarding your ET proposal
- May or may not be tied to a particular product or regulatory application

### How:

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

## Regulatory Submission Meetings and Applications with ET Component

- To follow the established regulatory procedures for CDER submissions
- Pre-submission meetings, INDs, NDAs, supplements ANDAs, BLAs
- We encourage the practice of applicants/sponsors flagging the regulatory submissions for ET component



## Emerging Technology Case Study 1 : Continuous Pharmaceutical Manufacturing

- Pharmaceutical industries have been slow in adopting the continuous manufacturing paradigm
- Most drugs are manufactured using “batch” technology — the finished product is made after several stops and starts, involving a series of steps
- Each break in the “batch” manufacturing process causes inefficiency and delay with potential to introduce defects and errors

## Traditional 'Batch' Manufacturing

- All materials are charged before the start of processing and discharged at the end of processing
- Product collected after each unit operation
- Finished product tested off-line after processing is complete
- Actual processing time from days to weeks

## Continuous Pharmaceutical Manufacturing

- Unit operations (blending, granulation, compression, and film-coating) are continuous
- Process: Adjusted based upon in-process measurements
- Product: Flows between each unit operation and monitored during processing
- More reliable products: Uninterrupted process; faster production (processing time from minutes to hours)

## Continuous Manufacturing: Salient Considerations

- Definition of “batch”, and need for enhanced process understanding
- Defining representative sampling to consistently assure product quality over time
- Need for integration of analytical tools to the control system to support implementation of feed-back or feed-forward control
- Location of sampling probes; and implementation of multivariate analysis for determination of product quality

## Continuous Manufacturing: Advantages

- Increased efficiency; avoidance of scaling up-related complications
- On-line monitoring and control for increased product quality assurance in real-time
- Enhancing process reliability and flexibility
- Lower manufacturing and building costs (40% less)
- Reduced waste, energy consumption, and raw material use

## Continuous Manufacturing and Regulations

- No specific regulations or guidance for continuous manufacturing, other than the definition of “lot”
- **Definition of “batch”:** Batch refers to the quantity of material and does not specify the mode of manufacture
- **Nothing in regulations or guidance to prohibit implementing continuous manufacturing**

FDA’s Recent Approval: First prior approval supplement for the introduction of a continuous manufacturing process for PREZISTA® Oral Tablets (treatment of HIV-1 infection)

# Continuous Manufacturing: Changing the Mind Set

**Present**



Traditional Batch Process Manufacturing



ETT to contribute towards  
promoting manufacturing  
innovations

**Future**



**Continuous Manufacturing/PAT**

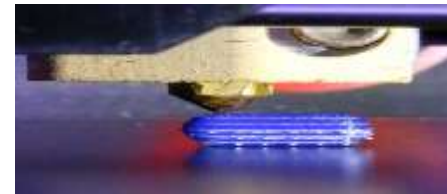


**Looking at the future of pharmaceutical manufacturing**

## Emerging Technology Case Study 2 : 3-D Printing Technology



### 3-Dimensional (3-D) Printing Technology



- ✓ **3-D Printing (additive manufacturing):** Layer-by-layer production of 3D objects from digital designs
- ✓ **3-D Printing versatility:** Successive layers of material formed under computer control to create an object. With a change in the underlying digital model, the same 3-D printing equipment can print a variety of products
- ✓ **Major innovations:** Bioengineering, drug manufacturing, prosthetics and medicine (Bioprinting)



## FDA Approval (2015) for First 3-D Printed Tablet: A Landmark Event



- Reformulation of antiepileptic levetiracetam
- The powder-liquid 3-D printing technology was developed at MIT
- A high drug load in a single dose in the form of porous, rapidly disintegrating, easy-to-swallow tablet
- No tablet compression used, tablet hardness considered a CQA for this porous tablet



250-1000  
mg

## 3-D Printing Technology: Scope and Long-Term Promise

- Superiority over conventional drug manufacturing paradigm
- On-demand manufacturing, personalized drug design
- Flexibility to add greater product design complexity
- Driving major innovations in tissue engineering, drug manufacturing, and personalized medicine
- “3-D printing signals the beginning of a third industrial revolution”

## Emerging Technology Case Study 3 : Digital Medicine/Ingestible Sensor Technology

**Medication non-adherence:** 40-50% of patients with chronic diseases in developed countries do not take medicines as prescribed--\$100-300 billion in avoidable health care cost

FDA Cleared (in 2015) Proteus® Ingestible Sensor Device with Adherence Monitoring Claim



Proteus® Ingestible Sensor Device:  
One-square- millimeter sensor in a pill coated in two digestible metals

## Digital Medicine: A Drug/Device Combination/Smart Pill



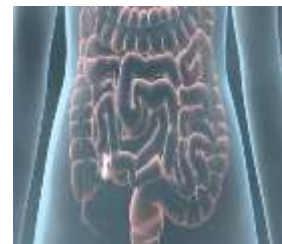
**Smart Pill Concept:** When patients ingest pills embedded with the tiny sensors, thin layers inside the circuit react with gastric fluid and trigger an electrochemical reaction that powers the sensor. The sensor then transmits a digital code to the patch worn by the patient

### Major Regulatory Considerations

- Failure mode analysis evaluation
- Evaluation of *in vivo* and 'real world' performance

## Wireless Diagnostic Imaging, and Patient Medication Adherence Monitoring

- **Battery-powered camera pill:** To take high-speed photos of the intestinal tract (PillCam<sup>®</sup> COLON for non-invasive colonoscopy)
- Camera transmits images to a data recorder, as capsule travels through the GI tract.
- **Smart Pill Bottle:** Currently being developed; lights up, buzzes and sends text and voice messages to remind users of dosage schedule, no of pills left; and bottle opening and closing history



# Oh, No it Finally Happened. I am Out of Ideas of Innovation



*Thank You!*