The Emerging Technology Program: FDA’s Perspective

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OVERVIEW

✓ Pharmaceutical Innovation: Challenges and Promises

✓ FDA Initiative: The Emerging Technology (ET) Program

✓ Emerging Technologies (In Public Domain): Sample Case Studies
  - 3-D Printing
  - Continuous Manufacturing
  - Novel Long-Acting Oral Drug Delivery
“Translational Gap”: Challenges of Developing Viable Innovative Technologies

Novel Discoveries/Conceptual Breakthroughs

“Translational gap”

Cost-Effective Novel Therapeutics

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 Program

• ET Evaluation: Principle of rigorous science-based assessment of innovative technologies while balancing risk vs. benefit

• ET draft guidance: Published earlier; currently getting revised
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 throughout the product lifecycle.

- By definition, ET will generally be unfamiliar, in both industrial and regulatory contexts, hence with limited or no regulatory precedence.
Contacting the Emerging Technology Team (ETT)

How:

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

When:
– **Early Stage of Development**: ET proposal may or may not be tied to a particular product or regulatory submission
– **Advanced Stage of Development**: Pre-submission meetings for regulatory applications with ET component (INDs, NDAs, ANDAs etc)
ET Case Study 1: 3-D Printing Technology

- 3-D Printing (additive manufacturing): Layer-by-layer production of 3D objects from digital designs

- 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: porous, rapidly disintegrating, easy-to-swallow tablet
- No tablet compression used, tablet hardness considered a CQA for this porous tablet
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”
ET Case Study 2: Continuous Pharmaceutical Manufacturing

Pharmaceutical industries have been slow in adopting the continuous manufacturing paradigm

Traditional “Batch Technology”

- Used to manufacture most drugs
- The finished product is made after several stops and starts, involving a series of steps
- Finished product tested off-line after processing is complete
- Each break causes inefficiency and delay with potential to introduce defects and errors (processing time: 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)
Poor adherence to prescription medication: health care cost ~ $100 billion

Emerging Frontiers in Drug Delivery

- Ultra long-acting, sustained release formulations
- Based on published work from MIT
- Long-Acting ingested capsule that, upon entering the stomach, assumes a geometry that prevents passage through the GI tract, enabling prolonged gastric residence
- Current extended and sustained release technologies achieve therapeutic serum levels for up to 12-24 hours.
- Emerging technology trends aims to push this timeline out to more than a week (Single Pill)