Examining Drug Quality Regulation

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Public Meeting on 21 CFR 314.70
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Intent of Meeting

- FDA is evaluating how it could revise its regulations to allow for consideration of risk-based approaches based on manufacturing process understanding, including prior knowledge of similar products, and overall quality systems to provide an enhanced risk-based approach to the CMC regulatory process, which would reduce the number of supplements.

Need to Reexamine Our Regulatory Approach to Drug Product Quality

- Need to ensure that pharmaceutical quality is sustained as technology evolves
- Need to ensure regulation does not impede new developments while still assuring product quality
- Need for greater efficiency given workload and available FDA/ industry resources

Desired State: A Mutual Goal of Industry, Society, and the Regulators

A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight.

Janet Woodcock, M.D.
October 5, 2005

Characteristics of Desired State

- Manufacturers develop and apply extensive knowledge about critical product and process parameters and quality attributes
- Manufacturers strive for continuous improvement
- FDA role: initial verification, subsequent audit
- Fewer manufacturing supplements needed

Janet Woodcock, M.D. -- CMC Workshop (October, 2005)

Accomplishing the Desired State

- Development of a new system to assess pharmaceutical manufacturing:
  - Build quality in - not test it - “quality by design” which changes application and inspection focus
  - Focus on manufacturing science
  - Focus on product risk and its relevance to quality
  - Improved interaction between review and inspection

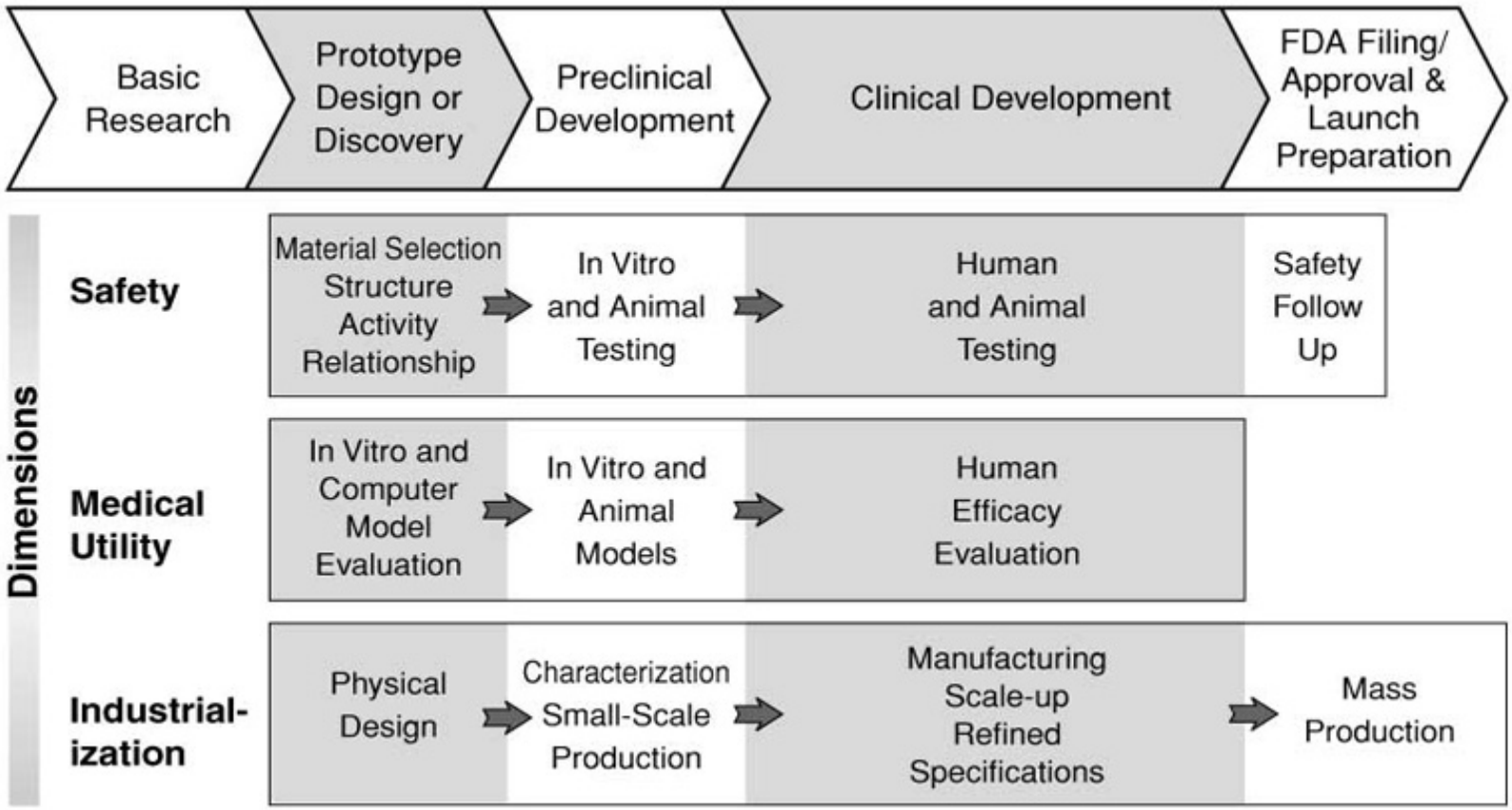
Consistent with FDA's Pharmaceutical cGMP Initiative

- Risk-based approach, goal of modernizing regulation of pharmaceutical manufacturing and product quality
- Quality Systems framework facilitating:
  - Consistent production of high quality, safe and efficacious product
  - Use of change control and continuous improvement
  - Use of quality by design (building quality into process and product)
  - Adoption of risk management approaches
  - Harmonization with other quality systems (within FDA and internationally)

Consistent with FDA's Role in the Critical Path Initiative

A serious attempt to focus attention on modernizing the evaluation of safety, efficacy and quality of medical products as they move from product selection 'discovery' to marketing 'delivery'

Critical Path - Importance of Industrialization



FDA's Role in Improving Manufacturing Regulation

- FDA's has a significant role in enhancing product development and manufacturing
  - Involved in review during product development -- we see the successes, failures, and missed opportunities
  - Open to new paradigms of manufacturing that assure continued product quality
  - Not a competitor but instead can serve a crucial convening and coordinating role for consensus development between industry, academia and government
  - Encourage innovation
- FDA working to improve the regulatory process

21 CFR 314.70: Need for Discussion

- 314.70 does not recognize recent developments in manufacturing science:
  - Risk management activities
  - Internal quality systems
  - Prescriptive and rules based
- While 314.70 is effective in ensuring quality for consumers, it may limit:
  - Productivity
  - Process control innovation
  - Flexibility

21 CFR 314.70: Potential Changes

- Leverage the advances in manufacturing science to reduce the need for review of low risk manufacturing changes (hence, reducing or eliminating need for supplements)
  - Greater flexibility for manufacturers to make timely, low-risk changes to manufacturing process
  - More efficient use of resources by manufacturers and FDA
    - FDA resources focused on manufacturing issues that could pose a significant risk

Summary

- Evolving manufacturing science promises a new approach to ensuring product quality, with a goal of efficient and agile manufacturing and regulation of pharmaceuticals
- Requires industry and FDA confront the assumptions that have guided manufacturing assessment previously
- Consistent with other Agency initiatives to foster innovation
- Focus on improving regulatory efficiencies while maintaining product quality
  - FDA progress in developing new directions and new regulatory processes to implement changing focus
- **Need public and manufacturer input to help identify potential targets for consideration and to help guide regulatory change**