

Nanotechnology and the FDA Critical Path Initiative

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Briefly Today

- FDA mission and strategic vision
- Critical path initiative
- Critical path application to nanotechnology
in medical products
- What is needed from you at this workshop

FDA Regulated Products

- Foods
 - All interstate domestic and imported, including produce, fish, shellfish, shell eggs, milk (not meat or poultry)
 - Bottled water
 - Wine (<7 alcohol)
 - Infant formula
- Food additives
 - Colors
 - Food containers
- Cosmetics
- Dietary Supplements
- Animal Feeds
- Pharmaceuticals
 - Human
 - Animal
 - Tamper resistant packaging
- Medical devices
- Radiation emitting electronic products
- Vaccines
- Blood and blood products
- Tissues
- Sterilants
- Counter-terrorism products

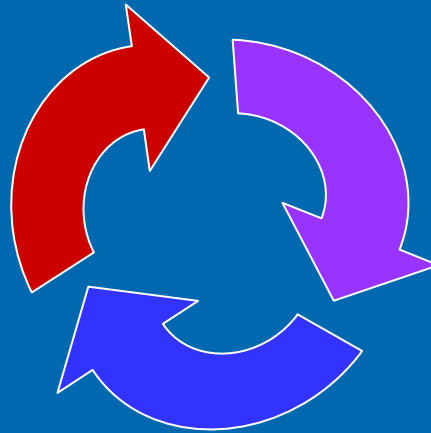
FDA's Core Business Functions

Pre-Market Review

Assessment of safety and effectiveness of new medical technology & safety of new food ingredients

Product Safety & Compliance

Inspection of manufacturing facilities and products to assure safety, quality & compliance with FDA regulations



Consumer & Patient Safety

Post-marketing surveillance to ensure the safety of consumers & patients who use FDA-regulated products

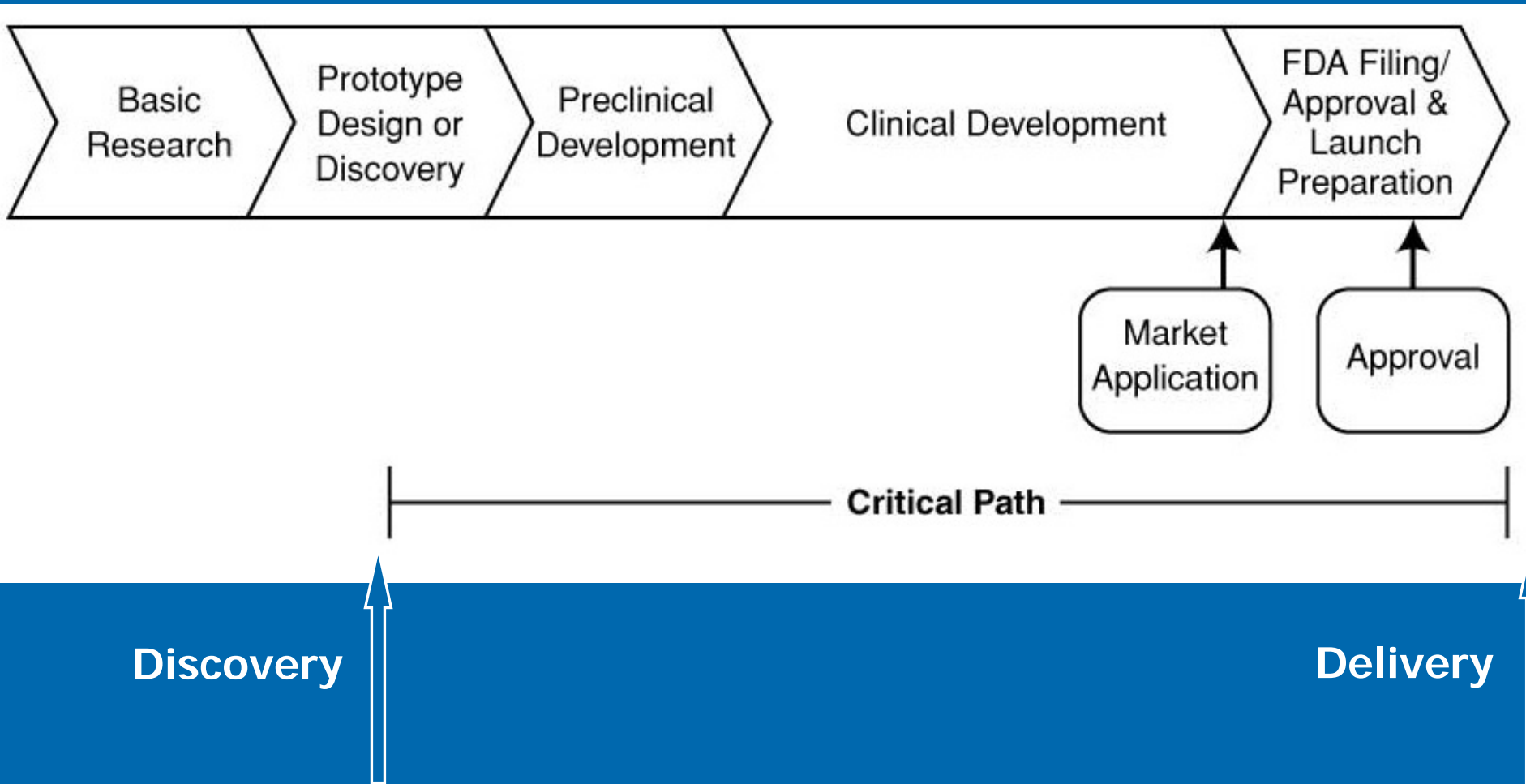
Our Vision for FDA Operations in the 21st Century:

- Safe Use of Marketed Products
- Innovation in Product Development and Access to New Technology
- Product Safety, Security, and Quality
- Business Transformation

Critical Path Initiative: Conceptual Framework

- Drug and medical device discovery and development in the 2000s did not appear to be producing at the expected level both in terms of quantity and quality (amount of information produced)
- Multiple explanations had been offered by various experts
- *Critical Path* offered a new explanation:
- ***lack of investment in development sciences***

The Critical Path for Medical Product Development



Critical Path Projects Designed to:

- Improve product quality and safety
 - e.g., quality by design, Severe Adverse Events Consortium
- Decrease regulatory uncertainty
 - e.g., new guidances, disease models & clinical trial simulation (Parkinson's, Non-Small Cell Lung Cancer)
- Increase quality of regulatory decisions
 - e.g., biomarkers (Non Hodgkin's lymphoma, nephrotoxicity)
- Increase flow of new, more effective and safer drugs for patients
- These projects should positively impact the development of nanotechnology products

Approach to Date

- Critical Path emphasizes collaborative ways of accomplishing objectives
- Funds are scarce, so pool resources, especially those that have been underutilized (i.e., data from development programs)
- Use industry data generated during compound development in a collaborative and pre-competitive manner
- Use NIH-funded trials and research to help qualify promising biomarkers

FDA Efforts to drug development uncertainty

(Critical Path)

Project	Potential Impact
Oncology Biomarker Qualification Initiative • Non Hodgkin's Lymphoma • Non-small cell lung CA	<ul style="list-style-type: none">• Better efficacy definition• Early go/no go• Tool linking pre-New Drug Application (preNDA) to clinical use
Severe Adverse Events Consortium (SJ Syndrome)	<ul style="list-style-type: none">• Predict and avoid adverse reaction• Improve benefit-risk for new drugs
Predictive Safety Testing Consortium	<ul style="list-style-type: none">• Predict drug induced nephrotoxicity pre-Investigational New Drug application (preIND)• Understand toxicity site
Cardiac Safety Consortium (QT _c Torsades)	<ul style="list-style-type: none">• Predict cardiac toxicity & sudden death

What is the Vision for Future Drug Development?

- Preclinical toxicology and clinical development move from empirical evaluations to quantitative, model-based, learn-confirm cycles
- Links between preclinical and clinical development data
- Predictive capacity of development system greatly enhanced
- Amount of information generated by system greatly increased

Nanotechnology and Critical Path

*“The Critical Path Opportunities List and Report”
(2006)*

Collaborative effort with stakeholders to:

- Create evaluative and predictive tools
- Stimulate Innovation
- Facilitate regulatory review
 - toxicology tests
 - imaging protocols
 - nano-platform for diagnostic tests
 - nano-platform for drug delivery

What Is New About Nanotechnology?

- FDA Nanotechnology Task Force Report (2007)
- Nanotechnology will bring products having multiple, integrated functions
 - For example, disease diagnosis, drug targeting, and non-invasive imaging elements are being combined in individual nanotechnology products
- Products will exploit “particle” based on physical properties in addition to “chemical” based properties, for example
 - Particle size is being used to target
 - Physical characteristics (e.g., heat retention) coupled with targeting

Exciting Public Health Benefits

- New treatments – not possible before
 - Solubility/absorption changes “bringing back” development candidates
 - Totally new concepts possible – limited only by the science we have, and our imagination
- Lower toxicity – targeted delivery
- Combinations of therapies – more effective treatment approaches

Drugs, Devices & Diagnostics Employing Nanotechnology

- May be different because of their physicochemical properties which will impact:
 - Absorption, Distribution, Metabolism, Excretion
 - Ability to detect, formulate & manufacture
- FDA will need to anticipate these new attributes in products in regulatory review, guidances, and education
- A goal of this workshop within the CPI framework is to help foster the development of a transparent, consistent, and predictable regulatory pathway for such products.

Authority vs. Guidance and CPI

- Authority
 - Manufacturers must demonstrate safety and efficacy of medical products to us before they can be marketed
- Guidance and consultation
 - In guidance and early consultation, we can indicate how data could be generated so that it would meet our decision needs about safety and efficacy
 - We want to communicate our decision and data needs clearly and predictably
 - Through CPI and Public Private Partnerships (PPP's), we want to take the further step of helping build the science, tools, and methods that reduce the time and cost needed to demonstrate safety and efficacy

What kinds of information do we need?

We'll hear from the 3 FDA centers that have medical product review responsibilities in areas of

- Product quality assessment studies
 - Characterization
 - Quality control
 - Manufacturing
- Product safety assessment studies
 - Biodistribution
 - Clearance
 - Metabolism
 - Toxicology

Likely Impact on Regulatory Review

Topic	Likely Different	No Impact
CMC	X	
Toxicology	X	
ADME, PK	X	
Dose	X	
Clinical Safety	X	
NDA Approval Endpoints		X

How we can use information like we will get from the projects?

- Knowledge that helps us consistently ask the right questions early in the process.
- It will encourage quality by design approaches
- To help ensure that the data that arrive will be appropriate to the review needs
 - Instruments and methods that can show biodistribution of relevant nanoscale particle properties
 - Assays that can screen and characterize toxicity and efficacy for nanoscale particles
 - Analytic methods that can show the critical specifications and impurities

Generally speaking,

what data should be generated,

what tools should be/could be developed,

what methods should be/could be developed and validated

ahead of time

so that we are better prepared when the products are ready for review?

What should be in the descriptions of projects you produce here?

- What is the issue to be solved?
- A description of the project.
- How generally applicable are the expected results?
- What data output elements and study design elements are critical?
- What is the timeline and general level of effort expected for the project?

How does it all fit together?

- Build combined efforts – focus on medical applications of the “Venn diagram” of PPP’s and data development efforts
- Alliance for NanoHealth – primary focus for this effort today – take advantage of the talent and capacity
- Use a “Coalition of PPP’s” approach to build complimentary solutions
 - NIH NanoHealth Enterprise
 - NCI’s Nanotechnology Characterization Laboratory
 - International Council on Nanotechnology
 - Safer Nanomaterials and Nanomanufacturing Initiative [SNNI]
 - Organization of Economic Cooperation and Development testing program
 - FDA Reagan-Udall Foundation
 - Others...

When and how?

- Today and tomorrow – for the very concrete, practical projects
- Then work with us to use the multiple pathways for finding the right solutions
 - Leveraging and sharing the load – not competing
- Help to build the solutions to getting it done

In Summary

- Very exciting new treatment opportunities for public health
- Looking ahead and working together, we can help speed them to patients
- Developing the critical path needs and solving them now is a shared goal

Thank you