



The FDA Critical Path Initiative – Opportunities and Challenges

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2006 CARDIOVASCULAR BIOMARKERS AND
SURROGATE ENDPOINTS SYMPOSIUM

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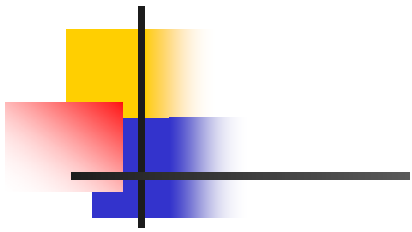


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Agenda

- Critical Path: What happens after 'Opportunities'?
- Role of biomarkers in development of novel cardiovascular therapeutics
- Role of the FDA in supporting development of novel biomarkers



Innovation

Stagnation

**Critical Path
Opportunities List**



U.S. Department of Health and Human Services
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Critical Path Opportunities List

FOR IMMEDIATE RELEASE

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FDA Unveils Critical Path Opportunities List Outlining Blueprint To Modernizing Medical Product Development by 2010

Biomarker Development and Clinical Trial Design Greatest Areas for Impact

Health and Human Services (HHS) Secretary Mike Leavitt and HHS' Food and Drug Administration (FDA) today released an initial list of priority research projects that could advance innovation in medical products. The announcement of the Critical Path Opportunities List signals the next major step in FDA's Critical Path Initiative, aimed at modernizing medical product development, so new medical discoveries are brought to patients faster and at a lower cost.

The Opportunities List outlines an initial 76 projects to bridge the gap between the quick pace of new biomedical discoveries and the slower pace at which those discoveries are currently developed into therapies. The release of the list marks a starting point in identifying priorities to be accomplished under the Critical Path Initiative. Government, industry and academic experts estimate that, if accomplished, the new tests and tools developed under the Critical Path Initiative will modernize the drug development process by 2010 and help to get new medical discoveries to patients faster and at a lower cost.

<http://www.fda.gov/oc/initiatives/criticalpath>



Critical Path Opportunities List: Six Areas of Focus

- **Better Evaluation Tools**
- Streamlining Clinical Trials
- Harnessing Bioinformatics
- Moving Manufacturing into 21st Century
- Developing Products to Address Urgent Public Health Needs
- Specific At-Risk Populations -
Pediatrics



Better Evaluation Tools: Biomarkers

- Historically, biomarker development unfocused, inefficient, siloed
- Development has focused on establishing surrogacy (difficult process)



Payoffs for Greater Use of Biomarkers

- Better dosing based on drug metabolism information
 - Selection of optimal dose
- Better definition of disease subsets
 - Reflect current clinical state of patients
 - Enhanced probability of success ('targeted therapy')
 - Goal of personalized medicine
- Prevention of adverse events
- Response monitoring



Future Biomarker Development and Use are Tightly Linked, More Efficient

- Novel biomarkers implemented and used throughout preclinical and clinical development
 - Need: ongoing discussions about the use of biomarkers throughout the development
 - Pre-IND, EOP2(a) meetings
- Biomarker/Surrogate development focused, efficient, cross-therapeutic class
 - Need: Clear pathway for biomarker development and regulatory approval
 - Need: Support for studies needed to qualify biomarkers:
 - Requires government-academic-industry collaboration and focus
 - Communication, sharing of results across drug areas



Role of FDA in Supporting Biomarker Development

- FDA participation in consortia to further overall biomarker development
 - Agency and CDER organization to support Critical Path
- Biomarker Qualification
 - Process issue
- Safety biomarkers important focus
- CDER Activities to support biomarker development



FDA Consortia to Support Biomarker Development

- Guiding Principles:
 - Multiple interested parties (FDA, PhRMA, academics, vendors)
 - No one group has all needed resources to move biomarker development forward efficiently
 - Cooperation can lead to more efficient product development than siloed biomarker use
 - Coordinated sharing needed to protect commercial interests while still allowing maximal sharing of information
 - Common language needed (i.e., data structure)



Biomarker Qualification

- Need pathway to qualify biomarkers, share results
- Example: Biomarker Consortium involving NIH Foundation, FDA, PhRMA
 - Wide range of biomarkers being evaluated for clinical qualification
 - Steering groups evaluating areas of interest: cancer, CV disease two examples
 - Oncology initiative will be demonstration project for larger initiative (FDG-PET)
- Other consortia around specific disease areas
- Guidance development



Focus on Safety Biomarkers

- Pre-competitive?
- Electronic ECG database Consortium
 - Started with new standard for electronic data submission of ECG waveforms
 - Partnership with FDA, academics (Duke), private groups (Mortara) and Pharma to identify/forward CV safety assessment
- Nephrotoxicity Biomarkers Consortium
 - Focused on pre-clinical markers of toxicity
 - Consortium between FDA, sponsors and academics (set up by C-Path Institute)
 - Help identify regulatory needs to support biomarker development



CDER Support of Critical Path and Biomarkers: Reorganization

- Office of Translational Sciences
 - Headed by Shirley Murphy, M.D
 - Includes Office of Biostatistics, Office of Clinical Pharmacology
 - Expertise central to Critical Path science
 - Facilitate Critical Path & research activities in CDER
 - Serve as focus for communications from interested outside groups and across FDA
 - Help identify/ prioritize CDER Critical Path activities

Future Vision of Biomarkers in Efficient Product Development



- Disease present?
- Receptor subtype present?

2D6 cypP450 genotype

- Cell, protein, antibody, small MW chemical, physical measure
- Linked to endpoint outcome for efficacy or toxicity

- [Drug]_{plasma(free)}
- Inhibitory concentration 90%

- PET, MRI,...
- Physical direct evidence for change

Incorporated into Disease Modeling...



Conclusions

- More systematic development and use of biomarkers is critical to efficient product development and use
- FDA actively supporting biomarker development
 - FDA Critical Path one effort to harness industry/academia/regulatory authorities to further:
 - Biomarker development through consortia, data sharing
 - Biomarker acceptance and use



Conclusions

- While barriers exist to greater integration of biomarkers into development, the status quo is not an acceptable future
 - FDA committed to making regulatory changes to support the efforts of academics and sponsors
- Progress in biomarker development will improve:
 - Drug development process efficiency, timeliness and predictability
 - Drug safety and effectiveness
 - Treatment outcomes for patients
 - Health care quality



Ultimate Goal of Critical Path, including Biomarker Initiative

"We are approaching an era of personalized medicine and nutrition, delivering the right treatment to the right patient at the right time...FDA will be the bridge to the development required by that future."

-----Andrew von Eschenbach, M.D.

Acting Commissioner for Food & Drugs

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