FDA: PAVING THE PATHWAY FOR INNOVATION

The Critical Path Initiative

The Critical Path Initiative activities generally involve long-term, science-based efforts to develop new tools (e.g., biomarkers, assays) and technologies (e.g., information technologies) that can be used during FDA-regulated product development, evaluation, manufacturing, and use. Collaboration plays a key role in many Critical Path efforts because success depends on bringing together the expertise and resources of all relevant stakeholders. A number of Critical Path activities involve the application of bioinformatics. It should be noted that although FDA has supported this effort largely through existing resources, in fiscal year 2008, Congress appropriated $7.5 million to support Critical Path projects in all FDA centers; more than $3.5 million was awarded to outside contractors to support Critical Path projects.

A Record of Accomplishment

FDA helped launch and participates in numerous partnerships and initiatives to tackle Critical Path hurdles. Recent examples include:

- ***The Clinical Trial Transformation Initiative (CTTI),*** a public-private partnership led by FDA and Duke University to modernize the clinical trial enterprise in the United States.

- ***The Sentinel Initiative,*** including multiple pilots that will directly inform FDA's Sentinel Initiative to develop and implement a nationwide electronic system for monitoring drug safety. Key examples include:
  - FDA-CMS-ASPE Pilot on electronic drug safety surveillance (using Medicare data).
  - OMOP (Observational Medical Outcomes Partnership with FNIH, FDA, PhRMA) to assess the value, feasibility, and utility of observational data to electronically identify and evaluate the safety risks and potential benefits of prescription drugs.
  - eHealth Initiative (Collaboration with HealthCare System and Regenstrief Institute/Indiana Network for Patient Care and FDA as advisor) to explore opportunities for using clinical information captured in the electronic databases of large health information exchanges to identify and assess safety signals associated with marketed pharmaceuticals.

- ***The Critical Path Institute (C-Path),*** a non-profit 501(c)3 organization, co-founded by the University of Arizona and the Stanford Research Institute (SRI) International, with input from the FDA, with the goals of accelerating safe medical product development and fostering education and training in applied research and regulatory sciences. Warfarin example:
  - FDA collaborated with C-Path and the University of Utah on the Cardiovascular Drug Safety and Biomarker Research Program to identify a pharmacogenetic algorithm to help improve the therapeutic efficacy and safety of warfarin dosing. As a result of this work, the labeling of warfarin has been updated. In a follow-on project, FDA is working with the National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI), third-party payers, and other thought-leaders in the field to identify what information would facilitate development of new genetic diagnostic tests for specific genotype-based dosing and drug-label recommendations for warfarin.

- ***The Oncology Biomarker Qualification Initiative (OBQI):*** FDA, NCI, and CMS are collaborating on key elements of a clinical trial protocol for FDG-PET, including programs in cancer imaging, development of molecular assays and targeted therapies, clinical trials, and data-mining in four areas: FDG PET in Hodgkin's Disease, breast cancer, lung cancer, and early detection of GIST.

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- ***The Predictive Safety Testing Consortium (PSTC)*** is sponsored by C-Path to bring together the Bristol-Myers Squibb Company, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Pfizer, Inc., Roche, Schering, Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Iconix, Sanofi-Aventis, and Wyeth to share precompetitive information on drug safety.

Strategies for the Future

- The Critical Path Initiative is a broad, long-term Agency-wide effort. The Office of Critical Path Programs (OCPP), Office of the Commissioner, provides human and fiscal resources in support of the many activities underway in the centers (e.g., helping to establish and manage collaborations, facilitate communication among the centers about Critical Path activities). In addition to continuing to support ongoing efforts, the OCPP is managing several key Agency-wide efforts that will remain high-priority projects for the coming decade. Key examples include:
    - ***The Clinical Trial Transformation Initiative***
    - ***The Sentinel Initiative***
    - ***Multiple information technology projects*** to transform FDA's paper-based data management approach to a wholly electronic environment:
        - Implement electronic establishment registration and drug listing systems
        - Develop a single portal and data repository for receiving adverse events and product problem reports
        - Expand the MedWatch program (i.e., MedWatch*Plus*)
        - Develop and implement an electronic platform for managing FDA-regulated product information
    - ***CAMD (Coalition Against Major Diseases),*** a collaboration to facilitate the development of treatments for diseases like Alzheimer's and Parkinson's.

Useful Resources

- ***The Critical Path website*** lists reports, upcoming events, and published articles on the Critical Path Initiative: www.fda.gov/oc/initiatives/criticalpath
- ***Information on the Sentinel Initiative:*** www.fda.gov/oc/initiatives/advance/sentinel
- ***Activities FDA launched or participated in during 2007:*** www.fda.gov/oc/initiatives/criticalpath/report2007.html
- ***Contact Information*** for the Office of Critical Path Programs: FDAcriticalpathprogram@fda.hhs.gov
- ***FDA Website:*** www.fda.gov