IOM Forum on Drug Discovery, Development & Translation

The FDA Response to the IOM Drug Safety Report

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Overview

- Our response to IOM report has three interconnected themes
  - Strengthening the science that supports our medical product safety system
  - Improving communication and information flows
  - Improving operations and management to strengthen the drug safety system
- Focus in response is on current authorities and resources
- Completion stages of these projects and additional IOM steps not part of current budget

CDER Initiatives - Strengthening the Science

- The scientific assessment of risks of medical products is at the core of our efforts to improve safety
- We are improving how we assess risks, how we manage them, and how we communicate with the public and healthcare professionals about risk

New Science of Safety

- New scientific discoveries are creating an emerging science of safety that will help us in lifecycle approach to drug saftey
  - "build safety in" as products are developed to screen out problematic compounds before they are widely tested in people
  - target patients who are likely to benefit from a product while protecting those who have no chance of benefit from being exposed
  - develop tests that can identify people at high risk for an adverse event
  - more rapidly and predictably detect problems once products are in medical use
  - move from emphasis on counting side effects - to emphasis on preventing and controlling them

Project - Pilot Program

Assess Safety Profiles of Newly Approved Products

- Pilot program:
  - Look at selected new molecular entities (NMEs) 18 months after approval
  - Review adverse events, datamining analyses, epidemiologic data, postmarketing clinical trial data, and Periodic Safety Update Reports to identify potential safety concerns
- Purpose of pilot is to evaluate whether such a look back can identify potential safety concerns early in the product life cycle.
- Not a “report card” on particular drugs
- Program is underway

Projects - Strengthening Epidemiologic Surveillance Methods and Tools

- IOM Response covered what we can do within current funding constraints
- Future much brighter.
- Upgrading electronic Adverse Event Reporting System
  - Incorporate latest tools such as datamining, signal detection and tracking
  - Make data more readily accessible to other public health agencies, researchers, public
- Increasing Safety Database Resources
  - Large databases maintained by public and private sectors (e.g., CMS, Kaiser) can:
    - enhance our ability to detect drug safety problems and medication errors
    - help us understand how products we regulate are used and factors that affect benefits and risks

Projects – Critical Path

- Develop quantitative methods for safety evaluation
- Develop and disseminate best practices for reviews of safety aspects of study protocols during product development
- Provide consistency in review practices and analytical approaches across review divisions to the extent possible
- Involved in an ongoing scientific collaboration intended to yield more sensitive, specific, and informative tests for drug organ toxicity

Projects – Critical Path (cont.)

- Collaborating with NIH, academia, industry, and other experts to develop a computer model
  - help researchers identify appropriate criteria for triggering early clinical intervention
  - identify patients most likely to suffer liver toxicity from specific compounds
- Working to validate preclinical (genomic) biomarkers of toxicity to use as experimental systems to test for the possibility of toxicity in humans
- Collaborating to develop a pharmacogenetic algorithm to help personalize dosing of warfarin
- Collaborating on project to determine how factors such as age, gender, and weight might influence patient response to warfarin

Improving Communication and Information Flow

- Improving our communication and information flows will further strengthen the effectiveness of the drug safety system
- Open and transparent communication among FDA, health care providers, and patients is key to rapid and effective dissemination of new information about safety issues

Transparent Decision Making is Critical

- Improving our use of Advisory Committees
  - Committees already provide open meetings, where the public can observe recognized scientific experts, with a diversity of views, review and discuss proposal, and provide advice
- Issuing new guidance documents to improve Advisory Committee operations by making them more consistent, transparent and predictable
- We will create a standard operating procedure for presenting postmarket safety issues to an Advisory Committee or other body, and
- Increase epidemiology expertise in Advisory Committee meetings

Projects - Communication

- Initiate 2 pilot projects
  - Evaluate Models of Involving OSE staff in reviews
  - Evaluate various models for more significant involvement in postmarketing decision making
- Proposed PDUFA IV recommendations include provisions for enhancing and improving communication and coordination between OSE and OND in CDER
  - Assess the impact and value of routinely including postmarket review staff on premarket review teams

Projects – Communication (cont.)

- Create new procedures to improve the decision-making processes related to postmarketing drug safety
  - Address issues such as how decisions are made to request further studies and labeling changes
- Implement an electronic system to track postmarket drug safety issues

New Advisory Committee

- Establishing a new advisory committee on communication to obtain input to improve the Agency's communication policies and practices
- Committee will include patients and consumers as well as experts in risk and crisis communication and social and cognitive sciences

Newsletter on Postmarketing Findings

- In 2007, we will begin to regularly publish a newsletter on the WEB containing:
  - summaries of results of FDA postmarketing reviews
  - Information on emerging safety issues
  - Information on recently approved products to inform providers and encourage reporting of adverse events to FDA
- Summaries will not include confidential commercial or pre-decisional information

Risk Communication

- Issued drug safety information guidance
  - Describes how we communicate important drug safety information, including emerging drug safety information, to the public
  - Formalizes our commitment and current efforts to ensure we provide the latest safety information with the potential to influence the way physicians prescribe and patients use drugs

Improving Operations and Management

- We agree with IOM on the need to improve the culture of safety at FDA and in CDER throughout the lifecycle of the products we regulate
- We are taking a number of steps, working with Dr. von Eschenbach, to effect a true culture change that will strengthen the drug safety system

Improving Operations and Management

- Specific steps:
  - Reinvigorate senior management team and charge them with leading in an integrated manner that crosses organizational lines
  - Enlist external organizational consultants to address concerns about lack of mutual respect and tension between pre-approval and post-approval staff
  - Clarify roles and responsibilities of pre- and postmarket staff so drug safety is better integrated into regulatory decision making at all stages of the drug life cycle
  - Improve the way scientific disagreements are handled

Conclusions

- One of the driving forces for change in drug safety is our ability to harness the potential of emerging science and technology to develop the tools to implement change
- FDA is committed to a comprehensive, systematic approach to improving the drug safety system
- FDA will develop and use new scientific tools, improve communication surrounding benefit and risk balance and improve CDER culture.
- Will need participation of a broad coalition of people outside the agency to fulfill the promise of these recommendations.

Questions?

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