

# **IOM Forum on Drug Discovery, Development & Translation**

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## **The FDA Response to the IOM Drug Safety Report**

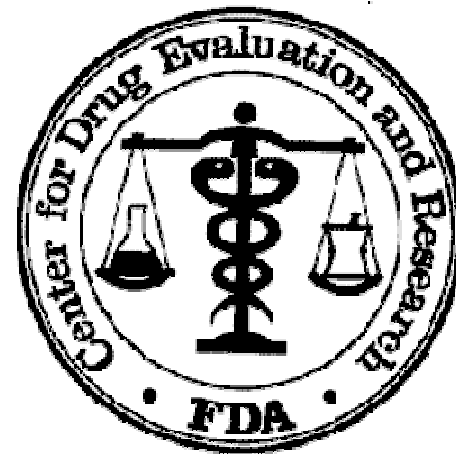
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**Food and Drug Administration**



# Overview

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



# CDER Initiatives - Strengthening the Science



- p The scientific assessment of risks of medical products is at the core of our efforts to improve safety
- p 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

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



# Project - Pilot Program

## Assess Safety Profiles of Newly Approved Products

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- p Pilot program:

- n Look at selected new molecular entities (NMEs) 18 months after approval
- n Review adverse events, datamining analyses, epidemiologic data, postmarketing clinical trial data, and Periodic Safety Update Reports to identify potential safety concerns

- p Purpose of pilot is to evaluate whether such a look back can identify potential safety concerns early in the product life cycle.

- p Not a “report card” on particular drugs

- p Program is underway

# Projects - Strengthening Epidemiologic Surveillance Methods and Tools

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- p IOM Response covered what we can do within current funding constraints
- p Future much brighter.
- p Upgrading electronic Adverse Event Reporting System
  - n Incorporate latest tools such as datamining, signal detection and tracking
  - n Make data more readily accessible to other public health agencies, researchers, public
- p Increasing Safety Database Resources
  - n 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

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

# Projects – Critical Path (cont.)

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- p Collaborating with NIH, academia, industry, and other experts to develop a computer model
  - n help researchers identify appropriate criteria for triggering early clinical intervention
  - n identify patients most likely to suffer liver toxicity from specific compounds
- p Working to validate preclinical (genomic) biomarkers of toxicity to use as experimental systems to test for the possibility of toxicity in humans
- p Collaborating to develop a pharmacogenetic algorithm to help personalize dosing of warfarin
- p 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

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- p Improving our use of Advisory Committees
  - n 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
- p Issuing new guidance documents to improve Advisory Committee operations by making them more consistent, transparent and predictable
- p We will create a standard operating procedure for presenting postmarket safety issues to an Advisory Committee or other body, and
- p Increase epidemiology expertise in Advisory Committee meetings

# Projects - Communication

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- p** Initiate 2 pilot projects

  - n** Evaluate Models of Involving OSE staff in reviews
  - n** Evaluate various models for more significant involvement in postmarketing decision making
- p** Proposed PDUFA IV recommendations include provisions for enhancing and improving communication and coordination between OSE and OND in CDER

  - n** Assess the impact and value of routinely including postmarket review staff on premarket review teams

# Projects – Communication (cont.)

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

# New Advisory Committee

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

# Newsletter on Postmarketing Findings

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



# Risk Communication

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- p** Issued drug safety information guidance
  - n** Describes how we communicate important drug safety information, including emerging drug safety information, to the public
  - n** 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



- p 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
- p 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

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## p Specific steps:

- n Reinvigorate senior management team and charge them with leading in an integrated manner that crosses organizational lines
- n Enlist external organizational consultants to address concerns about lack of mutual respect and tension between pre-approval and post-approval staff
- n 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
- n Improve the way scientific disagreements are handled

# Conclusions

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- p 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
- p FDA is committed to a comprehensive, systematic approach to improving the drug safety system
- p FDA will develop and use new scientific tools, improve communication surrounding benefit and risk balance and improve CDER culture.
- p Will need participation of a broad coalition of people outside the agency to fulfill the promise of these recommendations.





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# Questions?

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