Symposium on the Future of Drug Safety – Challenges for FDA

March 12, 2007
Hotel Monaco, Paris Ballroom
700 F Street NW, Washington, DC

Agenda

Symposium Objective: The Institute of Medicine recently released a report, *The Future of Drug Safety: Promoting and Protecting the Health of the Public*. This report includes recommendations for improving the U.S. drug safety system. These recommendations would likely entail significant new commitments for an agency that some consider to be financially strained by existing responsibilities. The meeting will consider the types and magnitudes of resources needed to achieve the goals of the IOM report. It will focus on a subset of IOM recommendations (attached) which were deemed to have significant resource implications—these are grouped into 5 topic areas: increased FDA funding; integration of pre and post market review; enhancing post market safety monitoring; conducting confirmatory drug safety and efficacy studies; and enhancing post market regulation and enforcement. The complete list of recommendations can be found in the Report or the Executive Summary at **http://www.nap.edu/catalog/11750.html**. For each topic, presenters will describe the relevant IOM recommendations, the FDA's current capacities and initiatives; and the resource implications of those recommendations.* Perspectives will include FDA officials (for information on current operations and plans), industry, patient advocates, and other experts.

7:30 am Coffee/Refreshments

8:00 am Welcome

GAIL CASSELL, SYMPOSIUM CHAIR AND MODERATOR
Co-Chair, Forum on Drug Discovery, Development, and Translation
Vice President, Scientific Affairs and Distinguished Lilly Research Scholar for Infectious Diseases
Eli Lilly and Company

* Please refer to the attached list for the full text of the recommendations cited.

Note: FDA participation is limited to providing background information on current FDA operations and plans

Session 1: Preserving the Public Trust: Ensuring Drug Safety, Efficacy, and Availability

Session Objectives: The IOM Drug Safety report recommended that the FDA receive "substantially increased resources" to support improvements in the system for ensuring drug safety and efficacy (**Recommendation 7.1***). This session will provide an overview of the role of the FDA in protecting the public, and the magnitude of resources appropriate to the task, from the perspectives of a former Secretary of Health and Human Services, a former FDA Commissioner, and an advocate for patients. In addition, the FDA's official response to the IOM recommendations will be presented.

8:10 am Ensuring commitment to safety through a strong FDA.

TOMMY THOMPSON
Honorary Chairman
Coalition for a Stronger FDA
Former Secretary for Health, U.S. Department of Health and Human Services

8:20 am Reflections on the historical challenges of regulating drug safety and efficacy.

JANE HENNEY
Senior Vice President and Provost for Health Affairs
University of Cincinnati Academic Health Center
Former Commissioner of Food and Drugs, U.S. Food and Drug Administration

8:30 am Preserving public trust in the drug safety regulatory system.

ELLEN SIGAL
Chairperson
Friends of Cancer Research

8:40 am The FDA response to the IOM Drug Safety Report.

STEVE GALSON
Member, Forum on Drug Discovery, Development, and Translation
Director, Center for Drug Evaluation and Research
U.S. Food and Drug Administration

8:50 am **Q & A**

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Session 2: Integration of Pre and Post Market Review

Session Objectives: The IOM Drug Safety report recommends adoption of a lifecycle approach to drug review, including integration of pre and post market review (**Recommendations 3.4, 4.4, 4.5, 4.13, and 5.4***). This session will describe the FDA's drug review process, the IOM recommendations for implementing a lifecycle approach to drug safety review, and the levels and types of resources needed to address the IOM report goals. In addition, the session will consider approaches to strengthening the scientific basis of pre market review.

9:05 am Overview of Key IOM Recommendations & Introductions

ALTA CHARO, PANEL MODERATOR
Member, IOM Drug Safety Committee
Professor
University of Wisconsin

Panel: Each panelist will make brief remarks followed by a Q&A period at the conclusion of the presentations.

9:15 am Operational challenges for instituting a lifecycle approach to drug review.

HUGH TILSON
Clinical Professor, Public Health Leadership
UNC School of Public Health

9:25 am Building FDA's capacity for science-based pre market review.

GARRET FITZGERALD
Member, Forum on Drug Discovery, Development, and Translation
Professor of Medicine, Professor and Chair of Pharmacology, Department of Pharmacology
University of Pennsylvania School of Medicine

9:35 am Current FDA initiatives to integrate pre and post market review.

BOB TEMPLE
Director, Office of Drug Evaluation
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

ELLIS UNGER
Deputy Director for Science (Acting)
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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9:55 am Industry's role in the institution of a lifecycle approach to drug safety review.

TIM FRANSON
Vice President, Global Regulatory Affairs
Lilly Research Laboratories
Eli Lilly and Company

10:05 am **Q & A**

10:35 am Break

Session 3: Enhancing Post Market Safety Monitoring

Session Objectives: The IOM Drug Safety report recommends significant changes in the FDA's post market review process (**Recommendations 4.1, 4.2, and 4.6***). This session will describe the FDA's current initiatives, the IOM recommendations for improving post market monitoring and drug safety review, and discuss the resources required to achieve the goals of the IOM report. Presentations will also consider ways to leverage existing resources to enhance post market safety monitoring, including the innovative use of databases and resources from other agencies, health plans, and industry.

10:50 am Overview of Key IOM Recommendations & Introductions

ANDY STERGACHIS, PANEL MODERATOR
Member, IOM Drug Safety Committee
Professor of Epidemiology and Adjunct Professor of Pharmacy
University of Washington

Panel: Each panelist will make brief remarks followed by a Q&A period at the conclusion of the presentations.

11:00 am FDA initiatives for improving drug safety monitoring.

GERALD DAL PAN
Director, Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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11:10 am Innovative use of existing data bases to aid in drug safety monitoring.

MARK MCCLELLAN
Visiting Senior Fellow
AEI Brookings Joint Center for Regulatory Studies
Former Commissioner of Food and Drugs, U.S. Food and Drug Administration

11:20 am Mining health plan patient data for drug safety monitoring.

RICHARD PLATT
Professor and Chair
Harvard Medical School and Harvard Pilgrim Health Care

11:30 am Leveraging non-FDA resources for drug safety surveillance.

BARBARA ALVING
Acting Director, National Center for Research Resources
National Institutes of Health

11:40 am Feasibility of implementing new approaches to enhance post market safety monitoring.

ALEC WALKER
Senior Vice President for Epidemiology
i3 Drug Safety, Ingenix

11:50 am Industry initiatives for utilizing health care data.

RON KRALL
Member, Forum on Drug Discovery, Development, and Translation
Senior Vice President and Chief Medical Officer
GlaxoSmithKline

12:00 pm **Q & A**

12:30 pm **Lunch / Roundtable Discussion**

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Session 4: Conducting Confirmatory Drug Safety and Efficacy Studies

Session Objectives: The FDA is limited in its ability to conduct studies on drugs that are already approved to assess the safety concerns or efficacy of drugs in clinical use. The IOM Drug Safety report calls for the development of public-private partnerships to prioritize, plan, and fund confirmatory drug safety and efficacy studies (**Recommendation 4.3*)**. Panelists will discuss the FDA's current capacity to organize such studies, consider approaches to expanding this capacity, and examine the costs of implementing these approaches. In addition, the IOM recommendation calling for enhanced clinical trial registration will be discussed (**Recommendation 4.11***).

1:30 pm Overview of Key IOM Recommendations & Introductions

ANDY STERGACHIS, PANEL MODERATOR

Panel: Each panelist will make brief remarks followed by a Q&A period at the conclusion of the presentations.

1:40 pm Current FDA initiatives to expand research capabilities.

JANET WOODCOCK
Member, Forum on Drug Discovery, Development, and Translation
Deputy Commissioner and Chief Medical
U.S. Food and Drug Administration

1:50 pm Funding large research studies.

ROBERT CALIFF
Member, Forum on Drug Discovery, Development, and Translation
Director, Duke Translational Medicine Institute
Professor of Medicine
Vice Chancellor for Clinical and Translational Research
Duke University Medical Center

2:00 pm Enhancing the value of clinical trial registration.

DEBORAH ZARIN
Director, ClinicalTrials.gov
National Library of Medicine

2:10 pm An industry perspective on expanding the capacity for post market studies and regulation of ClinicalTrials.gov.

GRETCHEN DIECK
Senior Vice President, Safety and Risk Management,
Pfizer Inc

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2:20 pm **Q & A**

2:50 pm Break

Session 5: Enhancing Post Market Regulation and Enforcement

Session Objectives: The IOM Report calls for clarification or strengthening of existing authority to regulate drugs already on the market, new methods to address direct to consumer advertising, and sufficient enforcement tools to ensure that regulatory requirements imposed at or after approval are fulfilled (**Recommendations 5.1, 5.2, and 5.3***). This session will describe how FDA currently deals with concerns about drugs that are on the market, will consider various approaches to enhancing the FDA's ability to regulate drugs following approval, and will examine the resource implications for both the FDA and industry of alternative approaches.

3:05 pm Overview of Key IOM Recommendations & Introductions

ALTA CHARO, PANEL MODERATOR

Panel: Each panelist will make brief remarks followed by a Q&A period at the conclusion of the presentations.

3:15 pm Providing FDA with clear and unambiguous regulatory authority.

CHRIS SCHROEDER
Member, IOM Drug Safety Committee
Professor of Law and Public Policy Studies
Duke University School of Law

3:25 pm Effective use of existing FDA authorities.

PETER BARTON HUTT
Senior Counsel
Covington & Burling LLP

3:35 pm Anticipated impact of new regulations upon patient safety and access.

EVE E. SLATER
Director
Vertex Pharmaceuticals and Theravance, Inc.
Former Assistant Secretary for Health, U.S. Department of Health and Human Services

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3:45 pm Making resources for post market compliance a priority.

MARY PENDERGAST
President
Pendergast Consulting

3:55 pm Industry perspectives on enhanced regulatory authority.

MARLENE HAFFNER
Executive Director, Global Regulatory and Intelligence Policy
Amgen, Inc.

4:05 pm **Q & A**

Session 6: Drug Safety Regulation: Looking to the Future

Panelists will reflect on the challenges and opportunities for enhancing drug safety discussed throughout the day, and share their thoughts on the steps necessary to ensure the continued ability of the FDA to meet the challenge.

4:40 pm **MYRL WEINBERG**
President
National Health Council

4:50 pm **MARK MCCLELLAN**

5:10 pm **Q & A**

Closing Remarks

5:20 pm **GAIL CASSELL, SYMPOSIUM CHAIR**

5:30 pm Adjourn

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Selected Recommendations from the IOM Report, *The Future of Drug Safety*, Referred to in the Symposium[*]

Session 1: Preserving the Public Trust: Ensuring Drug Safety, Efficacy, and Availability

7.1: To support improvements in drug safety and efficacy activities over a product's lifecycle, the committee recommends that the Administration should request and Congress should approve substantially increased resources in both funds and personnel for the Food and Drug Administration.

Session 2: Integration of Pre and Post Market Review

3.4: The committee recommends that CDER appoint an OSE *(office of surveillance and epidemiology – postapproval safety review staff)* staff member to each New Drug Application review team and assign joint authority to OND (*office of new drugs – review NDA's and decide upon approval)* and OSE for postapproval regulatory actions related to safety.

4.4: The committee recommends that CDER assure the performance of timely and scientifically-valid evaluations (whether done internally or by industry sponsors) of Risk Minimization Action Plans (RiskMAPs).

4.5: The committee recommends that CDER develop and continually improve a systematic approach to risk-benefit analysis for use throughout the FDA in the pre-approval and post-approval settings.

4.13: The committee recommends that the CDER review teams regularly and systematically analyze all postmarket study results and make public their assessment of the significance of the results with regard to the integration of risk and benefit information.

5.4: The committee recommends that FDA evaluate all new data on new molecular entities no later than 5 years after approval. Sponsors will submit a report of accumulated data relevant to drug safety and efficacy, including any additional data published in a peer reviewed journal, and will report on the status of any applicable conditions imposed on the distribution of the drug called for at or after the time of approval.

[*] To see all 25 recommendations, refer to the Full Report or the Executive Summary at **http://www.nap.edu/catalog/11750.html.**

Session 3: Enhancing Post Market Safety Monitoring

4.1: The committee recommends that in order to improve the generation of new safety signals and hypotheses, CDER (a) conduct a systematic, scientific review of the AERS *(adverse event reporting system)* system, (b) identify and implement changes in key factors that could lead to a more efficient system, and (c) systematically implement statistical-surveillance methods on a regular and routine basis for the automated generation of new safety signals.

4.2: The committee recommends that in order to facilitate the formulation and testing of drug safety hypotheses, CDER (a) increase their intramural and extramural programs that access and study data from large automated healthcare databases and (b) include in these programs studies on drug utilization patterns and background incidence rates for adverse events of interest, and (c) develop and implement active surveillance of specific drugs and diseases as needed in a variety of settings.

4.6: The committee recommends that CDER build internal epidemiologic and informatics capacity in order to improve postmarket assessment of drugs.

Session 4: Conducting Confirmatory Drug Safety and Efficacy Studies

4.3: The committee recommends that the Secretary of HHS, working with the Secretaries of Veterans Affairs and Defense, develop a public-private partnership with drug sponsors, public and private insurers, for profit and not for profit health care provider organizations, consumer groups, and large pharmaceutical companies to prioritize, plan, and organize funding for confirmatory drug safety and efficacy studies of public health importance. Congress should capitalize the public share of this partnership.

4.11: The committee recommends that Congress require industry sponsors to register in a timely manner at clinicaltrials.gov, at a minimum, all Phase 2 through 4 clinical trials, where they may have been conducted, if data from the trials are intended to be submitted to the FDA as part of an NDA, sNDA, or to fulfill a post market commitment. The committee further recommends that this requirement include the posting of a structured field summary of the efficacy and safety results of the studies.

Session 5: Enhancing Post Market Regulation and Enforcement

5.1: The committee recommends that Congress ensure that the Food and Drug Administration has the ability to require such postmarketing risk assessment and risk management programs as are needed to monitor and ensure safe use of drug products. These conditions may be imposed both before and after approval of a new drug, new indication, or new dosage, as well as after identification of new contraindications or patterns of adverse events. The limitations imposed should match the specific safety concerns and benefits presented by the drug product. The risk assessment and risk management program may include:

a. Distribution conditioned on compliance with agency-initiated changes in drug labels.
b. Distribution conditioned on specific warnings to be incorporated into all promotional materials (including broadcast DTC advertising).
c. Distribution conditioned on a moratorium on direct to consumer advertising.
d. Distribution restricted to certain facilities, pharmacists, or physicians with special training or experience.
e. Distribution conditioned on the performance of specified medical procedures.
f. Distribution conditioned on the performance of specified additional clinical trials or other studies.
g. Distribution conditioned on the maintenance of an active adverse event surveillance system.

5.2: The committee recommends that Congress provide oversight and enact any needed legislation to ensure compliance by both the Food and Drug Administration and drug sponsors with the provisions listed above. FDA needs increased enforcement authority and better enforcement tools directed at drug sponsors, which should include fines, injunctions, and withdrawal of drug approval.

5.3: The committee recommends that Congress amend the Food, Drug and Cosmetic Act to require that product labels carry a special symbol such as the black triangle used in the UK or an equivalent symbol for new drugs, new combinations of active substances, and new systems of delivery of existing drugs. The Food and Drug Administration should restrict direct-to-consumer advertising during the period of time the special symbol is in effect.