

REPORT BRIEF • SEPTEMBER 2006

## THE FUTURE OF DRUG SAFETY: ACTION STEPS FOR CONGRESS

The Institute of Medicine's Committee on the Assessment of the U.S. Drug Safety System intends that the 25 recommendations in its report will bring the strengths of the preapproval process (data, regulatory authority, organizational function and capabilities, and resources) to the postapproval phase in order to fulfill a lifecycle approach to the study, regulation, and communication about the risks and benefits of drugs.

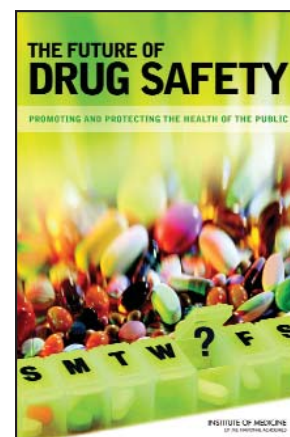
### CLARIFY FDA'S REGULATORY AUTHORITY

The Food and Drug Administration's authorities must be clarified and strengthened to empower the agency to take rapid and decisive actions when necessary and appropriate. FDA lacks the clear, unambiguous authority needed to enforce sponsor compliance with regulatory requirements and instead relies on the prospect of productive negotiations with industry.

5.1 The committee recommends that Congress ensure that FDA 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 FDA 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.



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## **REQUIRE SYMBOL TO ALERT CONSUMERS TO NEW PRODUCTS AND DENOTE HEIGHTENED REGULATORY ATTENTION**

Marking the label and all promotional material for newly approved drugs or indications with a special symbol will help increase awareness of the nature of newly approved therapies (for example, the incompleteness of information on safety).

- 5.3 The committee recommends that Congress amend the Federal 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. FDA should restrict direct-to-consumer advertising during the period of time the special symbol is in effect. The symbol should remain on the drug label and related materials for 2 years unless FDA chooses to shorten or extend the period on a case by case basis.

## **ESTABLISH PERFORMANCE GOALS FOR SAFETY**

The Prescription Drug User Fee Act mechanism that accounts for over half of the Center for Drug Evaluation and Research's funding and the reporting requirements associated with the user-fee program are excessively oriented toward supporting speed of approval and insufficiently attentive to safety.

- 3.5 To restore appropriate balance between the FDA's dual goals of speeding access to innovative drugs and ensuring drug safety over the product's lifecycle, the committee recommends that Congress should introduce specific safety-related performance goals in the Prescription Drug User Fee Act IV in 2007.

## **HOLD INDUSTRY AND RESEARCHERS ACCOUNTABLE FOR MAKING DRUG SAFETY STUDY RESULTS PUBLIC**

The committee believes strongly in the importance of increasing the availability of information to the public and to researchers about risks and benefits, whether specific study results or CDER staff analyses of concerns. The National Library of Medicine hosts a website for registration of clinical trials, but with few exceptions, this is voluntary and does not include a summary of results.

- 4.11 To ensure that trial registration is mandatory, systematic, standardized, and complete, and that the registration site is able to accommodate the reporting of trial results, the committee recommends that Congress require industry sponsors to register in a timely manner at [clinicaltrials.gov](http://clinicaltrials.gov), at a minimum, all Phase 2 through 4 clinical trials, wherever they may have been conducted, if data from the trials are intended to be submitted to the FDA as part of a new drug application, supplemental new drug application, 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.

## **APPROPRIATE ADEQUATE RESOURCES FOR DRUG SAFETY**

An agency whose crucial mission is to protect and advance the public's health should have adequate resources to do its job. Also, the effect on CDER's work of CDER's overdependence on PDUFA funding with restrictions on how FDA can use the money from user fees hurts FDA's credibility and may affect the agency's effectiveness.

- 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 FDA. The committee favors appropriations from general revenues, rather than user fees, to support the full spectrum of new drug safety responsibilities proposed in this report.

### **STABILIZE THE LEADERSHIP OF FDA**

Instability in the Office of the Commissioner has been a serious problem for FDA and CDER in particular. A large, complex, science-based regulatory agency cannot perform optimally in the absence of stable, capable leadership, and clear, consistent direction.

- 3.1 The committee recommends that the Federal Food, Drug, and Cosmetic Act be amended to require that the FDA Commissioner currently appointed by the President with the advice and consent of the Senate also be appointed for a 6-year term of office. The Commissioner should be an individual with appropriate expertise to head a science-based agency, demonstrated capacity to lead and inspire, and a proven commitment to public health, scientific integrity, transparency, and communication. The President may remove the Commissioner from office only for reasons of inefficiency, neglect of duty, or malfeasance in office.

### **IMPROVE FDA'S COMMUNICATION TO THE PUBLIC**

The public would benefit from more information about how drugs are studied before FDA approval, how drugs' risks and benefits are assessed, and what FDA review entails. Patients also need timely information about emerging safety concerns or about a drug's effectiveness in order to make better decisions in collaboration with their health care providers. FDA does not have an adequate mechanism for seeking and receiving specific scientific and patient/consumer advice on communication matters.

- 6.1 The committee recommends that Congress enact legislation establishing a new FDA advisory committee on communication with patients and consumers. The committee would be composed of members who represent consumer and patient perspectives and organizations. The advisory committee would advise CDER and other centers on communication issues related to efficacy, safety, and use during the lifecycle of drugs and other medical products, and it would support the centers in their mission to "help the public get the accurate, science-based information they need to use medicines and foods to improve their health."

### **OTHER RECOMMENDATIONS OF PARTICULAR INTEREST TO CONGRESS**

- 3.4 The committee recommends that CDER appoint an Office of Surveillance and Epidemiology staff member to each New Drug Application review team and assign joint authority to Office of New Drugs and OSE for postapproval regulatory actions related to safety.
- 4.10 The committee recommends FDA establish a requirement that a substantial majority of the members of each advisory committee be free of significant financial involvement with companies whose interests may be affected by the committee's deliberations.
- 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.

## FOR MORE INFORMATION...

Copies of *The Future of Drug Safety: Promoting and Protecting the Health of the Public* are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington Metropolitan area); Internet, <http://www.nap.edu>. The full text of this report is available at <http://www.nap.edu>.

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