

The Future of Drug Safety

PHARMACOVIGILANCE

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**IOM Committee on the Assessment of the US Drug
Safety System**



Some Committee Precepts (I)

- **An agency whose mission is “to promote and protect the health of the public” should not have to beg for resources to do its job.**
- *The FDA’s credibility is intertwined with that of industry, and a robust drug safety system is in everyone’s best interest.*
- **Safety and efficacy are the Yin and Yang of every drug and are best weighed together over the entire lifecycle of a drug.**



Some Committee Precepts (II)

- *Understanding of a drug's risks and benefits inevitably changes over the drug's lifecycle.*
- **Timely approval and attention to safety can and should become complementary rather than antithetical goals**
- *The timely identification, confirmation, and communication of risks and benefits are the best measure of regulatory success.*



The Report

- Culture, Structure and Management of CDER
- Quality and Quantity of the Science
- Credibility of the Science
- Regulation
- Communication
- Resources



What the Committee Did and Did Not Do

- The committee did *not* attempt to undertake a systematic review of specific drug safety incidents of recent years.
- The committee did attempt to focus on areas of vulnerability in the drug safety system and make recommendations for strengthening them



Vulnerabilities in the Drug Safety System

- Chronic underfunding
- Organizational problems
- Unclear regulatory authority and insufficiently flexible regulatory tools
- Inadequate quantity and quality of postapproval data, inadequate capability to systematically monitor drugs' risks and benefits postmarket



The Recommendations

- A suite of 25 recommendations that aimed to provide a cohesive, integrated approach to transforming drug safety:
- 8 directed to Congress
- 3 directed to the Secretary of HHS
- 14 directed to FDA/CDER



Key Messages

Carry the strengths of the preapproval process to the postapproval period

Adopt a lifecycle approach to drug risk and benefit

- In organization and functioning of CDER
- In terms of regulatory authority
- In the quality, quantity, and credibility of the science that underpins regulatory decision-making
- In communication with the public and patients



Resources

- Implementing the set of recommendations put forth in *The Future of Drug Safety* will require substantially increased resources.
- The committee strongly favors public funding, i.e., appropriations, but if that is not feasible, restrictions on use of PDUFA funds should be greatly reduced to allow management more flexibility to meet the agency's mission



CDER Structure and Organization: Recommendations

- A 6-year fixed term Commissioner to stabilize agency leadership, insulate it from some external pressures
- Appointment by DHHS Secretary of external Management Advisory Board to advise FDA Commissioner



CDER Structure and Organization: Recommendations

- A plan and support for cultural change
- Incorporation of safety goals into PDUFA goals letter
- Postmarketing safety staff be integrated into the drug review process and share post approval authority with drug review staff



CDER Structure and Organization: Recommendations

- Incorporating a lifecycle approach to risk and benefit into various aspects of CDER's culture and communicating that fact to all stakeholders could help bring speed and safety into optimal balance.
- Safety and efficacy must always be in balance, and the ideal organizational solution is a team approach to assessing both.



Regulatory Authority: Recommendations

- Congressional clarification of agency's enforcement authority
- Congressional authorization of a flexible and enforceable “tool kit” of regulatory options that may be applied at or after approval, e.g., conditions and restrictions on promotion and distribution, postmarketing studies



Regulatory Authority: Recommendations

- A special symbol on labels and promotional materials to remind providers and inform consumers that a drug is “new” and knowledge about its benefits and risks is limited
- FDA review of accumulated data on safety and effectiveness 5 years after the approval of a new molecular entity



Regulatory Authority: Take Home Message

Approval should not be the “last call” for realistic and effective regulatory action on drug safety.



The Science of Drug Safety: Recommendations

- Establish a public-private partnership to prioritize, plan, and organize funding for confirmatory drug safety, efficacy, and effectiveness studies
- Ensure scientifically valid and timely evaluations of Risk Minimization Action Plans



The Science of Drug Safety: Recommendations

- Register at clinicaltrials.gov all Phase 2-4 clinical trials if data are intended to be submitted to the FDA pre- or postmarket
- Post on a government website, such as clinicaltrials.gov, structured field summaries of results of all efficacy and safety studies



The Science of Drug Safety: Recommendations

- Post all NDA and sNDA review packages on FDA website
- CDER should regularly and systematically analyze all postmarket study results and make public their significance for the integration of risk/benefit information



Demonstrate Commitment to Research

- Appoint Chief Scientist in the Office of the Commissioner to oversee the quality and regulatory relevance of intramural and extramural research
- Include research capacity in FDA mission statement, and
- Request and apply resources to support intramural research, as approved by Chief Scientist



Advisory Committees

- Regularly include expertise in epidemiology and public health
- Review all New Molecular Entities prior to or shortly after approval



For More Information

- Report available at www.nap.edu
- Study Web site www.iom.edu/drugsafety
- Email Drugsafety@nas.edu

