- Involving OSE personnel in new drug reviews

In 2007, FDA is initiating two pilot projects to (1) evaluate various models of involving OSE staff in reviews, including the logistics and value of having an OSE staff person participate in each BLA and NDA review and (2) evaluate various models for more significant involvement of OSE in postmarketing decision making. The Agency is committed to ensuring that safety staff have a strong voice in pre- and postmarketing safety decision making. (***New***)

Furthermore, the proposed PDUFA IV recommendations also include provisions for enhancing and improving communication and coordination between OSE and OND in CDER and the Office of Biostatistics and Epidemiology and the premarket product review offices in CBER, including activities to assess the impact and value of routinely including postmarket review staff on premarket review teams. (***PDUFA IV Proposal***)

- Creating procedures to improve the decision-making processes related to postmarketing drug safety

Another outgrowth of the process improvement teams discussed above is the creation of new procedures to improve the decision-making processes related to postmarketing drug safety. These procedures will address issues such as how decisions are made to request further studies and labeling changes. ***(Recently initiated)***

- Creating an electronic postmarket drug safety tracking system

CDER is now implementing an electronic system to track postmarket drug safety issues. This system, which will replace multiple office- and division-specific systems, will enable CDER reviewers and managers to prioritize more effectively their work on safety issues and ensure that different organizational units have the same information. (***New***)

- Applying a quality systems approach to improve drug adverse event detection

We are strengthening and standardizing the process used by safety evaluators in OSE. These safety evaluators critically review adverse event reports that have been submitted to the Agency's AERS reporting system by sponsors of approved applications, healthcare professionals, consumers, and other sources. The goal of this initiative to strengthen the safety evaluation process is to identify best review practices and develop a quality assurance system including standardized methodologies, training and mentoring, workload prioritization, and management tools to optimize the use of resources to ensure efficient risk management. (***New***)

3. Improving our use of Advisory Committees

- Creating a standard operating procedure for presenting postmarket safety issues to an Advisory Committee or other body

This new procedure will articulate the division of responsibility between OND and OSE for planning, presentations, and Advisory Committee configuration and a process for compiling background materials for Advisory Committees. (***New***)

- Increase epidemiology expertise in Advisory Committee meetings

We also will increase the involvement, to the extent feasible, of pharmacoepidemiology and other experts in each Advisory Committee meeting when safety issues are an important component of the issues before the Committee. These individuals may be current members of the Drug Safety and Risk Management Committee (DSARM) or brought in as special government employees. (***New***)

- Strengthening FDA Advisory Committee management

The Agency will issue 3 guidances in 2007 making Advisory Committee operations more consistent, transparent, and predictable.

  - One guidance document will present new thinking about the criteria for granting waivers for conflicts of interest for members of all of our Advisory Committees.
  - A second guidance will address the disclosure of conflict of interest waivers.
  - A third guidance will improve the release of Advisory Committee briefing materials to the public.

In addition, we will make recruitment of potential members of Advisory Committees more transparent and open by issuing a standardized list of current and future Advisory Committee vacancies. (***New***)

IV. CONCLUSIONS AND NEXT STEPS

To achieve its statutory mission to promote and protect the public health, FDA relies on experts in science, medicine, and public health and on cooperation with patients, other consumers, and industry. FDA agrees with the IOM that our mission requires us constantly "to balance expeditious access to drugs with concerns for safety" (IOM Report p. S-2). FDA is fully committed to doing its part to improve continuously the quality of the U.S. drug safety system. But a drug safety system of the highest possible quality should not be confused with a system in which drugs are risk free. Because there are some risks whenever anyone uses a medication, safety considerations involve complex judgments by the healthcare community, patients, and consumers, who must constantly weigh the benefits and the risks before deciding to use a medical product. The Agency agrees with the IOM that "understanding a drug's risk-benefit profile necessarily evolves over the drug's lifecycle" (IOM Report p. S-3).

The Agency has carefully considered the recent IOM recommendations, along with previous expert suggestions, for making needed advances in this system. FDA has begun to take the steps needed to (1) further scientific understanding of drug products' benefits and risks, (2) rely on this understanding for regulatory decisions about drug marketing, and (3) communicate this understanding to healthcare professionals, patients, and the public so that they can make prescribing decisions based on the best scientific information available.

In this report, the Agency has identified specific actions it can take now in this regard. FDA will track each of the actions (18 recently initiated, 14 new, and 8 PDUFA IV) described here and will report in one year on our progress. It should be emphasized

that FDA does not view or treat drug safety in a vacuum but recognizes the need to integrate the specific initiatives in this report with a holistic program of product quality. Other FDA initiatives, such as Critical Path and our information technology modernization, will substantially contribute to the success of an ongoing commitment to ensure the safety and efficacy of the products we regulate. It is our goal to create an iterative process for improving the quality of the drug safety system by supplementing and expanding these actions as new funding becomes available and as new ideas for improvements to our drug safety system are evaluated and accepted. The Agency remains committed to working with renewed vigor to advance the scientific understanding and regulatory approaches needed for the safe use of marketed medical products.

APPENDIX A — STATEMENT OF TASK FOR THE IOM

(From Box p. S-1 of the IOM Report)

In response to growing public concern with health risks posed by approved drugs, the FDA has requested that the IOM convene an ad hoc committee of experts to conduct an independent assessment of the current system for evaluating and ensuring drug safety postmarketing and make recommendations to improve risk assessment, surveillance, and the safe use of drugs. As part of its work the IOM committee will

- Examine the FDA's current role and the role of other actors (e.g., health professionals, hospitals, patients, other public agencies) in ensuring drug safety as part of the U.S. healthcare delivery system
- Examine the current efforts for the ongoing safety evaluation of marketed drug products at the FDA and by the pharmaceutical industry, the medical community, and public health authorities
- Evaluate the analytical and methodological tools employed by FDA to identify and manage drug safety problems and make recommendations for enhancement
- Evaluate FDA's internal organizational structure and operations around drug safety (including continuing postmarket assessment of benefit and risk)
- Consider FDA's legal authority for identifying and responding to drug safety issues and current resources (financial and human) dedicated to postmarketing safety activities
- Identify strengths, weaknesses, and limitations of the current system
- Make recommendations in the areas of organization, legislation, regulation, and resources to improve risk assessment, surveillance, and the safe use of drugs

APPENDIX B — SUMMARY OF IOM RECOMMENDATIONS AND FDA ACTIONS

IOM Recommendations	FDA Actions	For more detail see Response section and page
3.1 Amend FD&C Act to require 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.	**Not directed to FDA**	
3.2 Secretary of HHS appoint an external Management Advisory Board to advise the FDA commissioner in shepherding CDER (and all of FDA) to implement and sustain the changes necessary to transform the Center's culture by improving morale and retention of professional staff, strengthening transparency, restoring credibility, and creating a culture of safety based upon a life-style approach to risk-benefit.	FDA is engaging external management consultants to help CDER/FDA develop a comprehensive strategy for improving CDER/FDA's organizational culture. [18] On January 19, 2007, the Commissioner proposed the creation of the Office of Chief Medical Officer, which will oversee scientific operations for FDA.	C.1, p. 16 A, p. 6
3.3 Secretary of HHS direct FDA commissioner and CDER Director, with the assistance of the Management Advisory Board, to develop a comprehensive strategy for sustained cultural change that positions the agency to fulfill its mission, including protecting the public health.	**See response to 3.2.**	

[18] The actions listed are those most relevant to the specific IOM recommendation. Other related actions may not be listed.

IOM Recommendations	FDA Actions	For more detail see Response section and page
3.4 CDER appoint an OSE staff member to each NDA review team and assign joint authority to OND and OSE for post-approval regulatory actions related to safety.	In 2007, FDA is initiating two pilot projects to (1) evaluate various models of involving OSE staff in reviews, including the logistics and value of having an OSE staff person participate in each BLA and NDA review and (2) evaluate various models for more significant involvement of OSE in postmarketing decision making. The Agency is committed to ensuring that safety staff have a strong voice in pre- and postmarketing safety decision making.	C.2, p. 15
	As described under B.3 above, we have already created two process improvement teams that have made recommendations about specific ways to increase communications between review staff and drug safety staff. Their recommendations to (1) establish an Associate Director for Safety and a Safety Regulatory Program Manager in each OND review division within CDER and (2) conduct regular safety meetings between OSE and all of the OND review divisions are all now being implemented.	C.2, p. 15
	Another outgrowth of the process improvement teams discussed above is the creation of new procedures to improve the decision-making processes related to postmarketing drug safety. These procedures will address issues such as how decisions are made to request further studies and labeling changes.	C.2, p. 16
	The proposed performance goals under PDUFA IV also include provisions for enhancing and improving communication and coordination between OSE and OND in CDER and the Office of Biostatistics and Epidemiology and the premarket product review offices in CBER, including activities to assess the impact and value of routinely including postmarket review staff on premarket review teams.	C.2, p. 16
	CDER is creating a standard operating procedure for presenting postmarket safety issues to an Advisory Committee or other body. This new procedure will articulate the division of responsibility between OND and OSE for planning, presentations, and Advisory Committee configuration and a process for compiling background materials for Advisory Committees.	C.3, p. 16

IOM Recommendations	FDA Actions	For more detail see Response section and page
3.5 Congress should introduce specific safety-related performance goals in the Prescription Drug User Fee Act IV in 2007.	**The proposed recommendations for PDUFA IV include the following safety-related performance goals:** FDA would develop a plan to (1) identify, with input from academia, industry, and others from the general public, risk management tools and programs for the purpose of evaluation; (2) conduct assessments of the effectiveness of identified Risk Minimization Action Plans (RiskMAPS) and current risk management and risk communication tools; and (3) conduct annual systematic review and public discussion of the effectiveness of one to two risk management programs and one major risk management tool. FDA would post reports of these discussions on its Web site. In addition, FDA would hold a public workshop to obtain input from industry and other stakeholders regarding the prioritization of the plans and tools to be evaluated. FDA would publish a request for proposals from outside research organizations who would be interested in conducting research on determining the best way to maximize the public health benefits associated with collecting and reporting serious and nonserious adverse events occurring throughout a product's life cycle. Central to addressing this question are determining the number and type of safety concerns discovered by AE collection, the age of products at the time safety concerns are detected by AE collection, and the types of actions that are subsequently taken to protect patient safety. FDA would use PDUFA funds to obtain access to additional databases and to hire the additional epidemiologists and programmers we need to use these databases. Access to types of data other than spontaneous reports would expand FDA's capability to conduct targeted postmarketing surveillance, to look at effects of classes of drugs, and to detect signals. Access to data other than spontaneous reports is essential to the transformation of the drug	 A.1, p. 7 A.2, p. 8 A.2, p. 9

IOM Recommendations	FDA Actions	For more detail see Response section and page
	safety program.	
	FDA, with input from pharmacoepidemiologists in academia and industry, would develop guidance on conducting scientifically sound pharmacoepidemiologic studies using observational data based on large healthcare data sets. We would hold a public workshop the first year of PDUFA IV to identify best practices for observational epidemiologic studies using large healthcare data sets. CDER and CBER would then jointly develop and issue a draft guidance document that recommends epidemiology best practices for this type of study.	A.2, p. 9
	Under PDUFA IV, to improve safety assessments supporting new drug applications (NDAs) and biologics license applications (BLAs), FDA would develop guidance for industry on how to test, detect, and prevent safety problems during drug development. For example, FDA would develop the following guidances:	A.3, p. 12
	• *Guidance on clinical hepatotoxicity* to make recommendations on how to evaluate a drug for possible hepatotoxicity during drug development and how FDA will review an application to look for signs that a drug may be a significant hepatotoxin.	A.3, p. 12
	• *Guidance on enriched trial designs* to focus on approaches to enrich the clinical trial population to better define the efficacy and safety of the drug under development.	A.3, p. 12
	The proposed performance goals under PDUFA IV also include provisions for enhancing and improving communication and coordination between OSE and OND in CDER and the Office of Biostatistics and Epidemiology and the premarket product review offices in CBER, including activities to assess the impact and value of routinely including postmarket review staff on premarket review teams.	B.3, p. 13/C.2, p. 16

IOM Recommendations	FDA Actions	For more detail see Response section and page
In addition, IOM recommends that FDA prepare a summary analysis of the adverse drug reaction reports not previously identified, potential new risks, or known risks reported in the unusual number not previously identified within 18 months of drug launch or after exposure of 10,000 persons, whichever is later. Reports should be publicly available and posted on the agency's web site.	See Rec 5.4	
4.1 Conduct a systematic, scientific review of the AERS system, identify and implement changes in key factors that could lead to a more efficient system, and systematically implement statistical-surveillance methods on a regular and routine basis for the automated generation of new safety signals.	We are upgrading AERS II, the second release of the Adverse Events Reporting System database, a Web-accessible computer system, to add signal detection and tracking tools. These tools will allow safety reviewers to more efficiently and effectively identify and track safety signals from submitted adverse events reports. During the first year of PDUFA IV, if it is enacted, FDA would publish a request for proposals from outside research organizations who would be interested in conducting research on determining the best way to maximize the public health benefits associated with collecting and reporting serious and nonserious adverse events occurring throughout a product's life cycle. Central to addressing this question are determining the number and type of safety concerns discovered by AE collection, the age of products at the time safety concerns are detected by AE collection, and the types of actions that are subsequently taken to protect patient safety. Under the proposed PDUFA IV recommendations, we would use PDUFA funds to obtain access to additional databases and to hire the additional epidemiologists and programmers we need to use these databases. Access to types of data other than spontaneous reports would expand FDA's capability to conduct targeted postmarketing surveillance, to look at effects of classes of drugs, and to detect signals. Access to data	A.2, p. 8 A.2, p. 8 A.2, p. 9

IOM Recommendations	FDA Actions	For more detail see Response section and page
	other than spontaneous reports is essential to the transformation of the drug safety program. On March 7 and 8, 2007, FDA is sponsoring a public meeting to explore opportunities for linking private sector and public sector postmarketing safety monitoring systems to create a virtual integrated, interoperable Nationwide medical product safety network. Such a ***Sentinel Network*** could integrate existing and planned private and public sector databases to enable the collection, analysis, and dissemination of safety information about medical products to healthcare professionals and patients at point of care (i.e., in the clinic where this information is needed to make informed decisions about safe and effective treatments). FDA will engage the public and private sectors in a discussion of opportunities for public and private sector collaboration on activities that could develop the data collection and risk identification and analysis components of such a potential network.	 A.2, p. 9
4.2 To facilitate formulation and testing of drug safety hypotheses, CDER should increase intramural and extramural programs that access study data from large automated healthcare databases, include these program studies on drug utilization patterns and background incidence rates for adverse events of interest, and develop and implement active surveillance of specific drugs and diseases as needed in a variety of settings.	FDA would use PDUFA funds to obtain access to additional databases (see Rec. 3.5) In addition, outside of PDUFA IV, FDA has embarked on other initiatives to obtain access to data: • Data use agreement with the Agency for Healthcare Research and Quality (AHRQ) • FDA and Veterans Health Administration (VHA) to share information and expertise • Active monitoring and analysis of influenza vaccine safety Many of the critical path initiatives will also help in the formulation and testing of drug safety hypotheses: • Developing and qualifying techniques for predictive toxicology • Identifying cardiovascular risk of drugs • Preventing drug-induced liver injury • Using pharmacogenomic information to guide safer and more effective use of drugs	A.2, p. 8 A.2, p. 8-9 A.3, pp. 10-12

IOM Recommendations	FDA Actions	For more detail see Response section and page
	• Using new scientific tools to enhance blood safety • Enhancing the long-term safety of gene therapy	
4.3 The Secretary of HHS working with the Secretaries of Veterans Affairs and Defense should 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.	The Veterans Health Administration (VHA) and FDA are working under a recently signed memorandum of understanding to allow sharing of certain information related to the use of drugs, vaccines, other biological products, and medical devices. The purpose of the project is to enhance knowledge and efficiency through the sharing of information and expertise between FDA and VHA regarding medical product safety, effectiveness, and patterns of use.	A.2, p. 9
4.4 CDER should assure the performance of timely and scientifically-valid evaluations (whether done internally or by industry sponsors) of Risk Minimization Plans (RiskMAPs).	FDA would develop a plan to (1) identify, with input from academia, industry, and others from the general public, risk management tools and programs for the purpose of evaluation; (2) conduct assessments of the effectiveness of identified Risk Minimization Action Plans (RiskMAPS) and current risk management and risk communication tools; and (3) conduct annual systematic review and public discussion of the effectiveness of one to two risk management programs and one major risk management tool. FDA would post reports of these discussions on its Web site. In addition, FDA would hold a public workshop to obtain input from industry and other stakeholders regarding the prioritization of the plans and tools to be evaluated.	A.1, p. 7

IOM Recommendations	FDA Actions	For more detail see Response section and page
4.5 Develop and continually improve a systematic approach to risk-benefit analysis for use throughout the FDA in the pre-approval and post-approval settings.	On May 30 and 31, 2006, FDA and IOM held a workshop to hear about new proposals in quantitative benefit-risk assessment. FDA is continuing to explore the possible use of best practices in this area, with a goal of ultimately identifying and testing quantitative tools that could be of use. In the meantime, we have introduced several training courses to help medical reviewers conduct better safety assessments.	A.1, p. 7
	In 2006, CDER created the Quantitative Safety and Pharmacoepidemiology Group (QSPB) to promote science-based, data-supported, regulatory decisions on the safe use of medicinal therapeutics. This group of internal experts will develop quantitative methods for safety evaluation, develop and disseminate best practices for reviews of safety aspects of study protocols during product development, and provide consistency in review practices and analytical approaches across review divisions to the extent possible.	A.1, p. 7
	CBER (Center for Biologics Evaluation and Research) has implemented an integrated approach to benefit and risk analysis, including cross-cutting product safety teams, and has built a quantitative risk assessment unit that it uses for scientific and modeling support of its more mathematically complex, highest priority product and public health safety issues (e.g., it is being used for a quantitative assessment of risks of transmissible spongiform encephalopathy (mad cow disease) in plasma derived Factor VIII products). See pilot for NMEs (Rec 5.4) See also critical path initiatives (Rec. 4.2)	A.1, p. 7
	FDA and the National Toxicology Program of the National Institute of Environmental Health Sciences are developing and validating an animal model to examine factors that may increase the risk of cancer that has been associated with some gene therapies. The model can be used by sponsors to test modifications to gene therapy vectors to mitigate cancer risk while preserving effectiveness. In November 2006, FDA provided a new, risk-based guidance to sponsors on long-term follow up of such therapies.	A.3, p. 12

IOM Recommendations	FDA Actions	For more detail see Response section and page
	We are strengthening and standardizing the process used by safety evaluators in OSE. These safety evaluators critically review adverse event reports that have been submitted to the Agency's AERS reporting system by sponsors of approved applications, healthcare professionals, consumers, and other sources. The goal of this initiative to strengthen the safety evaluation process is to identify best review practices and develop a quality assurance system including standardized methodologies, training and mentoring, workload prioritization, and management tools to optimize the use of resources to ensure efficient risk management. CDER is now implementing an electronic system to track postmarket drug safety issues. This system, which will replace multiple office- and division-specific systems, will enable CDER reviewers and managers to prioritize more effectively their work on safety issues and ensure that different organizational units have the same information.	C.2, p. 16 C.2, p. 16
4.6 Build internal epidemiologic and informatics capacity to improve the postmarket assessment of drugs.	See access to databases in Recs. 3.5 and 4.2	
4.7 Commissioner should demonstrate commitment to building the agency's scientific research capacity by: Appointing Chief Scientist in OC to oversee, coordinate, ensure quality and regulatory focus of FDA's intramural research programs. Designate FDA's Science Board as the extramural Advisory Committee to the Chief Scientist. Include research capacity in agency's mission statement. Apply resources to support intramural research approved by the Chief Scientist. Ensure adequate funding to support	The Commissioner has requested that the FDA Science Board undertake a comprehensive formal review of scientific needs and activities across the Agency. The vast majority of FDA scientific programs are related to regulated product safety. See Rec. 3.2	A, p. 6

IOM Recommendations	FDA Actions	For more detail see Response section and page
intramural research program is requested in the agency's annual budget request to Congress.		
4.8 FDA should have its advisory committees review all NMEs either prior to approval or soon after to advise in the process of ensuring drug safety and efficacy or managing drug risks.	See pilot for NMEs (Rec 5.4)	
4.9 Advisory committees, and any other peer review effort such as mentioned for CDER-reviewed product safety, should include a pharmacoepidemiologist or an individual with comparable public health expertise in studying the safety of medical products.	We also will increase the involvement, to the extent feasible, of pharmacoepidemiology and other experts in each Advisory Committee meeting when safety issues are an important component of the issues before the Committee. These individuals may be current members of the Drug Safety and Risk Management Committee (DSARM) or brought in as special government employees.	C.3, p. 17
4.10 FDA should establish a requirement that a substantial majority of AC members be free of significant financial involvement with companies whose interests may be affected by the committee's deliberations.	Under the oversight of the recently confirmed FDA Commissioner, the Agency will issue 3 guidances in 2007 making Advisory Committee operations more consistent, transparent, and predictable. • One guidance document will present new thinking about the criteria for granting waivers for conflicts of interest for members of all of our Advisory Committees. • A second guidance will address the disclosure of conflict of interest waivers. • A third guidance will improve the release of Advisory Committee briefing materials to the public.	C.3, p.17

IOM Recommendations	FDA Actions	For more detail see Response section and page
	In addition, we will make recruitment of potential members of Advisory Committees more transparent and open by issuing a standardized list of current and future Advisory Committee vacancies.	
4.11 Congress should require industry sponsors to register in a timely manner at 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 an NDA, sNDA, or to fulfill a post-market commitment. Include a posting of structured field summary of efficacy and safety results of the studies.	**Not Directed to FDA**	
4.12 Post all NDA review packages on the agency's web site, including all supplemental NDA review packages.	**Not accepted**	B.6, p. 14
4.13 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.	FDA recognizes the importance of communicating information about the safety of drugs. However, many postmarketing assessments contain recommendations that are the subject of ongoing discussions within FDA and other information that is predecisional in nature. Release of such information could have adverse public health impacts. For example, release of information about a safety signal that is later determined to be erroneous could result in patients who could benefit from the drug not receiving it. Therefore, decisions to publicly disclose assessments of postmarketing safety studies have to be made on a case-by-case basis. In 2007, we plan to regularly publish a newsletter on the FDA Web site containing summaries of the results, including methods, of FDA postmarketing drug reviews. The summaries will not include confidential commercial or predecisional information. We believe it is important, particularly for healthcare professionals, for FDA to make	B.6, p. 14 B.5, p. 14

IOM Recommendations	FDA Actions	For more detail see Response section and page
	readily available and easily accessible the results of our postmarketing reviews of adverse events. In addition, this regular newsletter will contain information on emerging safety issues, as well as provide information on recently approved products both to inform providers and to encourage reporting to the Agency. In the first quarter of 2007, FDA will issue a final guidance on communicating important drug safety information, including emerging drug safety information, to the public. This guidance formalizes FDA's commitment and current efforts to ensure that it communicates to healthcare professionals, patients, and other consumers the latest safety information with the potential to influence the way physicians prescribe and patients use medicines.	B.4, p. 13
5.1 The committee recommends that Congress ensure that the Food and Drug Administration has the ability to require such post marketing risk assessment and risk management programs as 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.	**Not Directed to FDA**	
5.2 Provide oversight and enact any needed legislation to ensure compliance by FDA and drug sponsors with provisions listed above (5.1). FDA needs increased enforcement	**Not Directed to FDA**	

IOM Recommendations	FDA Actions	For more detail see Response section and page
authority and better enforcement tools directed at drug sponsors, which should include fines, injunctions, and withdrawal of drug approval.		
5.3: Amend FD&C Act to require 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 DTC advertising during the period of time the special symbol is in effect (recommended time: 2 years).	**Not Directed to FDA**	
5.4 Evaluate all new data on NMEs 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.	CDER is conducting a pilot developed by its Office of Surveillance and Epidemiology (OSE) and its Office of New Drugs (OND) to review systematically and collaboratively the safety profiles of new molecular entities (NMEs) on a regularly scheduled basis to determine whether these reviews should be initiated for all NMEs as suggested by IOM recommendation 5.4. NME postmarketing evaluations will incorporate data from the Adverse Events Reporting System (AERS), data mining analysis, epidemiologic data, postmarketing clinical trial information, and a review of the Periodic Safety Update Reports (PSURs), or U.S. Periodic Report, to identify potential safety concerns early in the product life cycle.	A.1, p.7
6.1 Enact legislation establishing a new Advisory Committee on communication with patients and consumers. The committee would be composed of members who represent consumer and patient perspectives and organizations. The AC would	We are establishing a new advisory committee to obtain input to improve the Agency's communication policies and practices and to advise FDA on implementing communication strategies consistent with the best available and evolving evidence. We will include on the Committee patients and consumers as well as experts in risk and crisis communication and social and cognitive sciences. The IOM report recommends that Congress enact legislation to establish a new Advisory	B.2, p. 13

IOM Recommendations	FDA Actions	For more detail see Response section and page
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 get the public accurate, science-based information they need to use medicines and foods to improve their health.	Committee on communication with patients, but we believe we can implement the IOM's recommendation more expeditiously through administrative procedures.	
6.2 Office of Drug Safety Policy and Communication should develop a cohesive risk communication plan that includes, at a minimum, a review of all Center risk communication activities, evaluation, and revision of communication tools for clarity, consistency, and priority-setting to ensure efficient use of resources.	We have established a working group, chaired by CDER's Associate Director for Safety Policy and Communication, to develop a CDER risk communication strategic plan. In the process of developing this plan, CDER will identify, clarify, and define the purpose of each communication tool and streamline the use of tools to facilitate information flow. As part of this process, CDER is also evaluating the CDER Web site and will implement changes to make it more efficient and effective. In addition, FDA's recently established Bioinformatics Board in the Office of the Commissioner has taken steps to improve the public's ability to communicate to FDA. The Bioinformatics Board has initiated an Agency-wide project to create a common portal for the collection of adverse event reports and consumer complaints about products for all FDA regulated products. The scope of this project includes developing mechanisms to improve the ease and accuracy of reporting by the public and to improve the timeliness and quality of reports submitted to the FDA.	B.1, p. 13
7.1 To support improvements in drug safety and efficacy activities over a product's lifecycle, Congress should approve substantially increased resources in both funds and personnel for the FDA.	**Not directed to FDA**	

ABBREVIATIONS

AC - Advisory Committee
AE - Adverse Event
AERS - Adverse Events Reporting System
AHRQ - Agency for Healthcare Research and Quality
ANDA - Abbreviated New Drug Application
BLA - Biologics License Application
CBER - Center for Biologics Evaluation and Research
CDC - Centers for Disease Control and Prevention
CDER- Center for Drug Evaluation and Research
CMS - Centers for Medicare & Medicaid Services
C-PATH - Critical Path Institute
CRADA - Cooperative Research and Development Agreement
DTC - Direct to Consumer (refers to DTC advertising)
DCRI - Duke Clinical Research Institute
DSARM - Drug Safety and Risk Management Committee
ECG - Electrocardiograms
FD&C ACT (also FDCA) - Federal Food, Drug, and Cosmetic Act
FDA - Food and Drug Administration
FOIA - Freedom of Information Act
HHS - Department of Health and Human Services
HIV - Human Immunodeficiency Virus
IOM - Institute of Medicine
NDA - New Drug Application
NHLBI - National Heart, Lung, and Blood Institute
NIH - National Institutes of Health
NME - New Molecular Entity (never before approved)
OC - Office of the Commissioner
OND - Office of New Drugs
OSE - Office of Surveillance and Epidemiology
PDUFA - Prescription Drug User Fee Act
PSTC - Predictive Safety Testing Consortium
PSUR - Periodic Safety Update Report
QSPB - Quantitative Safety and Pharmacoepidemiology Group

RFP - Request for Proposal

RiskMAP - Risk Minimization Action Plan

VHA - Veterans Health Administration

VSD - Vaccine Safety Datalink