DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98N–0339]

FDA Plan for Statutory Compliance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a document entitled ''FDA Plan for Statutory Compliance'' (the plan). This document is the agency's response to section 406(b) of the Food and Drug Administration Modernization Act of 1997 (FDAMA), which requires the Secretary of the Department of Health and Human Services (the Secretary) to develop a plan bringing the agency into compliance with the requirements of the Federal Food, Drug, and Cosmetic Act (the act).

DATES: Written comments may be submitted at any time.

ADDRESSES: Submit written comments on the plan to Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit e-mail comments to ''FDADockets@bangate.fda.gov''. E-mail comments should be labeled as comments and identified with the docket number found in brackets in the heading of this document.

Submit written requests for single copies of the ''FDA Plan for Statutory Compliance'' to the Dockets Management Branch (address above). Enclose one self-addressed adhesive label to assist that office in processing your requests. Copies of this plan are available on the Internet at ''http://www.fda.gov/opacom/7modact''.

FOR FURTHER INFORMATION CONTACT: Steven H. Chasin, Office of Planning and Evaluation (HFP–20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–5207.

SUPPLEMENTARY INFORMATION:

I. Background

On November 21, 1997, the President signed FDAMA into law. Section 406(b) of FDAMA requires the Secretary, after consultation with appropriate scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry, to develop and publish a plan bringing the Secretary into compliance with each of the obligations of the Secretary under the act. The plan is to be reviewed biannually and revised as necessary, in consultation with the groups listed in the previous sentence. The plan must address the following six objectives: (1) Maximizing the availability and clarity of information about the process for review of applications and submissions made under the act; (2) maximizing the availability and clarity of information for consumers and patients concerning new products; (3) implementing inspection and postmarket monitoring provisions of the act; (4) ensuring access to the scientific and technical expertise needed by the Secretary to meet the obligations of the Secretary under the act; (5) establishing mechanisms, by July 1, 1999, for meeting the time periods specified in the act for the review of applications and submissions made under the act and submitted after November 21, 1997; and (6) eliminating backlogs in the review of applications and submissions described previously by January 1, 2000.

Over the past several months, the agency held a series of meetings with its stakeholders. The process of consulting with agency stakeholders began with a careful examination of FDA's stakeholders vis-a-vis the products regulated by the agency and the perceived interest of these groups in FDA's processes. A total of eight open public meetings were held where agency stakeholders had an opportunity to provide their perspectives on a variety of issues/questions. Six of the eight meetings were focused specifically on FDA's product centers; one briefing for health professionals provided an opportunity for health professionals to offer input to FDA under the broad guidance of section 406(b) of FDAMA; and an agency-wide meeting was held to capture the perspectives of those who could not attend previous meetings and to provide an opportunity to explore recurring themes from previously held meetings.

In addition to the open public meetings focused specifically on section 406(b) of FDAMA, agency staff used a variety of ongoing interactions with stakeholders as opportunities to talk about the stakeholder consultation process and to invite comments to the docket.

II. The Plan

The agency plan for statutory compliance has been developed in response to the requirements outlined in section 406(b) of FDAMA. The plan presents a blueprint for carrying out all of the agency's statutory obligations, including provisions of the act, as well as its other mandates.

The plan outlines FDA's strategic directions for the next 5 years and presents an operational plan for fiscal year 1999 and 2000. The plan is a dynamic document which will be modified as ongoing consultations with FDA stakeholders render new and more effective strategies.

The act itself builds upon a long history of recommendations from advisory committee members, industry representatives, and consumers to help the agency respond to new challenges while still fulfilling its mission and mandates. It was Congress' belief that FDA could address these challenges by re-engineering several of its regulatory processes to achieve greater efficiencies and by buttressing its considerable risk assessment and risk management expertise through productive, collaborative relationships with key external stakeholders.

III. Comments

Interested persons, may at any time, submit written comments to the Dockets Management Branch (address above) regarding this plan. Two copies of any comments are to be submitted, except individuals may submit one copy. Comments should be identified with the docket number found in brackets in the heading of this document.

Submit e-mail comments to ''FDADockets@bangate.fda.gov''. E-mail comments should be labeled as comments and identified with the docket number found in brackets in the heading of this document. A copy of the document and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

The text of the plan follows:

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Food and Drug Modernization Act of 1997—FDA Plan for Statutory Compliance

November 1998

Table of Contnets

Executive Summary

Part One: Strategic Framework

Purpose
Scope
The Mandated Strategic Framework
FDA's Strategic Management Approach
- Mission Development
- Emerging FDA Challenges
- Analysis of the Gap Between What is Expected of FDA and Its Actual Performance
- Stakeholder Consultation
- Identification of Agency-wide Objectives and Strategic Directions

Part Two: FDAMA Plan for FY 1999
Objective A: Information about Review Processes
Objective B: Information about New Products
Objective C: Implementing Inspection and Postmarket Monitoring Provisions
Subobjective C1: Assuring Product Safety
Subobjective C2: Adverse Event Reporting
Objective D: Science and Research
Objectives E and F: Eliminating Backlogs
Appendices

Executive Summary: FDA Plan for Statutory Compliance

Purpose

The FDA Plan for Statutory compliance addresses requirements set forth in Section 406 of the Food and Drug Administration Modernization Act of 1997 (FDAMA). The Plan identifies those actions necessary to bridge the gap between what FDA is required to do by statute and what it is able to accomplish with current resources. FDAMA has presented FDA with an opportunity to close that gap by working in concert with its community of stakeholders to protect the health and well-being of the American public. This Plan is a positive first step. It outlines bold and innovative approaches to meet the increasingly complex public health challenges of the 21st century.

FDA, however, is unable to meet all of these challenges with its current level of resources. Innovation and creative collaboration with stakeholders will enhance this effort, but significant additional resources, as well as prioritization of FDA activities, are essential if FDA is to meet its statutory requirements on a sustained basis and to meet public expectations. The successful implementation of this Plan depends on commitment of resources by both FDA and its stakeholders.

Scope

The Plan specifically addresses each of the objectives stipulated by Congress in FDAMA Section 406(b). These objectives, when achieved, will result in the following outcomes: stakeholders who are well informed about and involved in the Agency's new products and regulatory processes; comprehensive monitoring of industry practices and product use; regulatory decisions that are supported by a sound science base; and on-time reviews of new products prior to market entry.

To accomplish these objectives the Plan outlines FDA's strategic directions over the next 5 years and specific performance goals for Fiscal Year (FY) 1999. The Plan was developed in close consultation with a wide range of stakeholders, including consumers and patients, industry, health professionals, and other public sector regulators. The end product represents the collective views of FDA's senior leaders and its community of stakeholders.

The Plan

FDA Challenges in Fulfilling Its Mission: FDA must address several key challenges now and in the future for the Agency to successfully meet its statutory requirements and to fulfill its health promotion and protection mission. These include: research and development-fueled pressures on regulatory responsibilities; greater product complexity driven by breakthroughs in technology; growth in recognized adverse effects associated with product use; unpredictable new health and safety threats; awareness of citizen-stakeholders and their more targeted needs; emerging regulatory challenges in the international arena; and increased volume and diversity of imports. The ability to formulate successful solutions to these challenges depends on innovative approaches used by FDA, creative collaboration with stakeholders, prioritization of FDA activities, and an adequate investment of resources to implement these approaches.

Stakeholder Views: FDA's senior leadership listened carefully to the viewpoints of its many stakeholders prior to the development of this Plan. These opinions were expressed during a series of public meetings held during the summer of 1998. Several productive suggestions surfaced from these discussions. Two general themes emerged:

(1) *Greater stakeholder involvement:* Stakeholders want to be ongoing contributors to FDA's future strategies. Effective collaboration can raise the likelihood that these strategies will be successful. Stakeholders also want to be well-informed about FDA's regulatory processes. Consumers and patients want clear information about new products, and they want to receive the information in a timely manner.

(2) *Balanced, risk-based FDA decisions:* Stakeholders agreed that FDA priorities should be risk-based, and also believe that the Agency should balance timely premarket review programs with the need for effective postmarket inspection and surveillance. They urged the Agency to continue to develop a strong scientific and analytical basis for regulatory decisions. Some urged FDA to rely more on third parties and others want more direct FDA regulation.

Current Innovations/Reinventions: While stakeholders have made useful suggestions for enhancing Agency programs, FDA had already begun steps to improve its approach to public health protection and is continuing this effort. This has been accomplished both through redesign of internal programs and via collaborative efforts with outside parties. New, critically important medicines are now reaching the market more rapidly as a result of more efficient Agency review processes and the automation of these processes. Since 1993, the medium approval time for new drugs has been substantially reduced, from 20 months to around 12 months in 1997. FDA is collaborating with its regulatory colleagues as well as the regulated industry to develop national systems of consumer protection. Two examples are cited: FDA is working closely with the U.S. Department of Agriculture, the Center for Disease Control and Prevention, and the states to develop a comprehensive network for ensuring safety of the American food supply. FDA is also coordinating with the international regulatory community and the U.S. Customs service to increase assurance that imports entering the country are safe.

Strategic Directions for the Future: FDA's senior leadership identified the following strategic directions in order to focus the Agency's energies on meeting the objectives set forth in the Plan:

- *Establish risk-based priorities*—Focus resources on those health and safety risks that most directly threaten the well-being of U.S. consumers.
- *Strengthen the scientific and analytical basis for regulatory decisions*—A strong science base must underpin each of the Agency's regulatory decisions.
- *Work more closely with external stakeholders*—Collaboration with stakeholders will result in more effective solutions to public health problems.
- *Continue to re-engineer FDA processes*—Re-engineering will result in regulatory simplification and more cost-effective ways to run FDA's internal processes.
- *Adopt a systems approach to Agency regulation*—Regulatory approaches in the future will look for total problem solutions, rather than piecemeal review and enforcement decisions.
- *Capitalize on information technology*—Information technology will help to improve both internal efficiency and communication with stakeholders.

The six strategic directions outlined above will guide FDA's efforts to meet the FDAMA objectives. Many factors over the next several years will have an impact on FDA's ability to meet these

objectives including the outcome of a risk-based priority system, the success of third parties in the regulatory process, improvements in technology and systems engineering, and the synergies created by greater collaboration with other federal agencies, as well as FDA's external stakeholders, new statutory mandates, and emerging public health responsibilities. Reinvention will enable FDA to make up some of the difference between current performance and FDAMA objectives. Additional resources will also be necessary over the next 5 years in order for the Agency to satisfy its statutory requirements and to meet public expectations.

The body of this Plan identifies the major areas where FDAMA calls for FDA to meet statutory requirements, such as premarket reviews, injury reporting, and product safety assurance. It also discusses areas where there are not statutory requirements, but where there is general agreement on what time frames for reviews and inspections are appropriate and what other work needs to be accomplished to meet FDAMA objectives. FDA would be hard pressed to meet all of the FDAMA objectives with current resources and operating procedures. For example, in FY 1999 the Agency estimates it can accomplish roughly one-half to three-quarters of its statutory inspectional workload with current funding (See FIGURE 3).

Plan Organization

Part One of the Plan, the strategic framework, provides the broad Agency-wide context of the Plan. This includes:

(1) development of a clear mission statement;
(2) assessment of challenges that FDA faces in fulfilling its mission;
(3) analysis to the gap between what is expected of FDA and its actual performance;
(4) consulting FDA's stakeholders on future directions; and
(5) a statement of Agency-wide objectives (Section 406(b)) and strategic directions to achieve the objectives.

Part Two of the Plan maps the specific plan for achieving each 406(b) objective, including strategies and performance goals that can be used to manage toward the objectives. In Part Two, the specific performance targets for FY 1999 are established based on the Agency's existing resources, reinventions, and collaborative arrangements. FY 2000 performance targets currently are being developed as part of the FY 2000 Budget process and are not included in the Plan.

Part One—Strategic Framework

Purpose

The FDA Plan for Statutory Compliance addresses requirements set forth in Section 406 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) (see Appendix A). The Plan identifies those actions necessary to bridge the gap between what FDA is required to do by statute* and expected to do by the public—and what the Agency currently is able to accomplish with existing resources. A high-performing FDA working in concert with its stakeholders is absolutely crucial to promote and to protect the health and well-being of the American public. Given the myriad escalating technological, economic, and health risk challenges, this will not be an easy task for FDA. The passage of FDAMA presents FDA with an opportunity to demonstrate innovative and bold approaches in meeting these challenges for the 21st century. This Plan is one positive step toward moving FDA into conformance with the views of Congress and the Agency's stakeholders.

This document demonstrates that FDA already is making great progress in managing health risks—a job that is becoming more complex and often fraught with uncertainty and unpredictability. The Plan also highlights the fact that the Agency clearly is unable to meet all of the challenges it is expected to address with its curent level of resources. Innovation and creative collaboration with external stakeholders will certainly enhance the Agency's abilities to reduce health risks in the long run; but additional resources are essential to help FDA fulfill its statutory mandates.

[*Statutory requirements encompass all provisions of the Federal Food Drug and Cosmetic Act (FD&C Act) and its amendments, including FDAMA.]

Scope

The Plan specifically addresses the six objectives stipulated by Congress in FDAMA Section 406(b):

- Maximize the availability and clarity of information about the process for review of applications and submissions.
- Maximize the availability and clarity of information for consumers and patients concerning new products.
- Implement inspection and postmarket monitoring provisions of this Act.
- Ensure access to needed scientific and technical expertise.
- Establish mechanisms, by July 1, 1999, for meeting time periods for the review of all applications and submissions.
- Eliminate backlogs in the review of applications and submissions by January 1, 2000.

To achieve these objectives, the Plan identifies Agency-wide strategic directions for the next 5 years, and specific performance goals for Fiscal Year (FY) 1999. Thus, the total plan presents a picture of the Agency's long- and short-term future that will be reviewed and modified as part of ongoing discussions with FDA's stakeholders, with future Department of Health and Human Services (DHHS) leadership and other parts of the Administration, and with Congress.

The Mandated Strategic Framework

This Plan is one element of a total strategic framework mandated by FDAMA that enables FDA to address increasingly complex public health challenges. This framework, outlined in Section 903 of the Federal Food, Drug, and Cosmetic Act as amended by FDAMA (see Appendix A), contains the following key elements:

1. An augmented mission statement for FDA, which places new emphasis on more resource-intensive consultation and cooperation with stakeholders as a crucial ingredient in public health protection and promotion [Sec. 903(b)(4)].
2. A charge to the Secretary of Health and Human Services to foster collaboration among science-based agencies throughout the federal government. Such coordination is necessary to strengthen the science capabilities that underpin federal responsibilities to ensure a safe food supply and related to development, evaluation, and monitoring of new medical therapies [Sec. 903(c)].
3. Stipulation of general powers that are necessary for carrying out Agency responsibilities, including research and education [Sec. 903(d)].
4. A requirement that FDA develop, after consulting with stakeholders, a plan for bringing the Agency into compliance with each of the obligations under the Act (The FD&C Act), and revise that plan as appropriate with stakeholder input [Sec. 903(f)].
5. A provision for FDA to prepare and publish an annual report that compares planned versus actual performance [Sec. 903(g)].

These elements reflect certain broad themes. First, the Agency should devise and implement strategies in a more open, multi-organizational environment. Congress emphasized throughout FDAMA that consultation, collaboration, and synergy-building

with external organizations are paramount to FDA achieving its mission of protecting and promoting public health. Simply put, FDA cannot do the job alone.

Second, Section 903 provides FDA with a more systematic approach to strategic management. The essential elements are clearly articulated: a clear mission, consultation with stakeholders, a plan based on stakeholder input to carry out the intent of the mission, and provision for ongoing feedback, accountability, and adjustment to the plan. The Agency recognizes the importance of this plan for action accountability, as outlined in Section 406(b) of FDAMA, and in establishing an ongoing dialogue with stakeholders to continually improve strategies.

Third, Congress has recognized that an array of capabilities including public education and research [Section 903(d)(2)] are essential elements required to carry out its responsibilities under the Act. The six objectives outlined in FDAMA 406(b) also explicitly stipulate education and scientific expertise as being central to the Agency's modernization plan. Successful public health promotion and protection decisions depend upon a well-developed science infrastructure and an informed public. Without these two elements, desired health outcomes are not possible.

FDA's Strategic Management Approach

Figure 1 illustrates how FDA is integrating the mandates in Section 903 to form the components of an effective strategic management process. As the figure illustrates, effective implementation of the FDAMA plan depends upon several elements:

(1) development of a clear mission statement;

(2) assessment of challenges that FDA faces in fulfilling its mission;

(3) analysis of the gap between what is expected of FDA and its actual performance;

(4) consulting FDA's stakeholders on future directions;

(5) a statement of Agency-wide objectives [406(b)] and strategic directions to achieve the objectives;

(6) a specific plan for achieving each 406(b) objective, including strategies and performance goals that can be used to manage toward the objectives; and

(7) a budget that adequately funds the plan.

Part One of the Plan provides the broad Agency-wide context—steps 1 through 5 above. Part Two of the Plan maps the specific plan for achieving objectives. In Part Two, the specific performance targets for FY 1999 are established based on the Agency's existing resources, reinventions, and collaborative arrangements. FY 2000 performance targets currently are being developed as part of the FY 2000 Budget process and are not included in the Plan. Many factors influence FDA's choice of performance levels, including: extrapolations of past performance, anticipated workload, creative re-engineering to improve internal efficiencies, successful collaboration with FDA's outside stakeholders, and strategic priorities.

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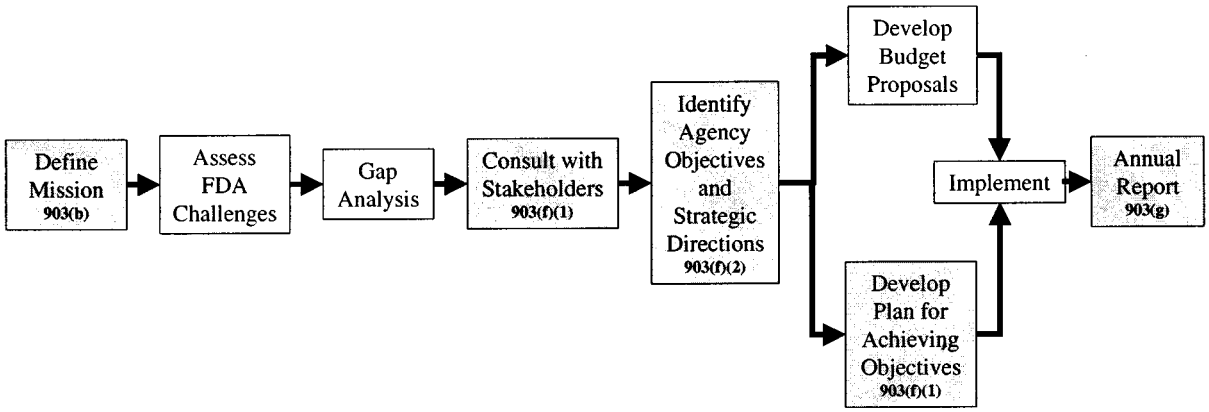
Figure 1: FDAMA's Refocus of FDA's Strategic Management Process

(Shaded areas are FDAMA changes to Section 903 of FFD&C Act)



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Mission Development

Over the years, Congress has dramatically expanded the responsibilities of the FDA. The Federal Food and Drugs Act of 1906, the first national statute enacted by Congress to regulate the American food and drug supply, gave FDA's predecessor agency the authority to remove adulterated or misbranded foods and drugs. In ensuing years, Congress enacted a series of statutes that expanded FDA's responsibilities in a number of directions, including: new product areas (cosmetics, biologicals, and medical devices.); additional product characteristics (e.g., efficacy as well as safety); and additional perspectives from which to monitor products (e.g., monitoring prior to market introduction as well postmarket monitoring).

Beginning in 1996 with the passage of the Animal Drug Availability Act (ADAA) and continuing in 1997 with the passage of FDAMA, Congress enhanced FDA's mission in ways that recognized the Agency would be operating in a 21st century characterized by increasing technological, trade, and public health complexities. To meet these challenges, Congress added explicit phrasing to the Agency's mission statement to ensure that FDA would coordinate its own efforts with regulatory counterparts worldwide. In addition, Congress recognized that external scientists, medical experts, and public health experts must play an increasing role in Agency responsibilities. It defined a new emphasis to be placed on regulatory processes and required more interaction with stakeholders. Through FDAMA, Congress intends to ensure timely availability of safe and effective new products that benefit the public, and to ensure that our nation continues to lead the world in new product innovation and development.

DAMA defines FDA's new mission as follows:

The Administration shall—

(1) promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner;

(2) with respect to such products, protect the public health by ensuring that—

(A) foods are safe, wholesome, sanitary, and properly labeled;

(B) human and veterinary drugs are safe and effective;

(C) there is reasonable assurance of the safety and effectiveness of devices intended for human use;

(D) cosmetics are safe and properly labeled; and

(E) public health and safety are protected from electronic product radiation;

(3) participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements; and

(4) as determined to be appropriate by the Secretary, carry out paragraphs (1) through (3) in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.

Emerging FDA Challenges

FDA must address a wide range of challenges that serve as potential obstacles to successfully carrying out its health protection mission in the 21st century. To the extent that these challenges remain unaddressed, a gap between expectation and performance will persist. This Plan represents a blueprint for addressing these challenges, thereby narrowing the gap.

Key challenges that FDA faces now and in the near future include:

1. Research and development-fueled pressures on regulatory responsibilities;
2. Greater product complexity driven by breakthroughs in technology;
3. Growth in recognized adverse effects associated with product use;
4. Unpredictable, new health and safety threats;
5. More targeted needs and awareness of citizen-stakeholders;
6. Emerging regulatory challenges in the international arena;
7. Increased volume and diversity of imports; and
8. Federal budget constraints.

Each of these challenges is discussed briefly below.

• Research and Development-fueled Pressures on Regulatory Responsibilities

Each year, FDA-regulated firms add more than $2 billion to domestic research and development efforts. For pharmaceuticals alone, this effort currently exceeds $20 billion total, which is triple the effort of only 10 years ago. The growth in research budgets at public agencies such as NIH surely will result in a greater number and wider variety of products that FDA must, by statute, regulate. More importantly, the speed of product development also is accelerating. By streamlining the commercial review process, FDA has helped to reduce the time between discovery and Agency evaluation. But this streamlining also gives the Agency very little time to develop a regulatory framework to handle new technologies. Thus, it is imperative for FDA to continue to engage in close interaction with industry in the early stages of product research and development.

The volume, variety, and speed of new product development presents FDA with the twofold goals of: (1) ensuring that consumers enjoy timely public health benefits from these products; and (2) minimizing the health risks associated with consumers' use of these products. FDA resources devoted to premarket review of these products must be carefully allocated so that *both* goals are addressed. The Agency's current level of resources, however, cannot adequately address both goals in all of the product areas for which the Agency has responsibility.

• Greater Product Complexity Driven by Breakthroughs in Technology

Product complexity continues to increase. FDA-regulated products will be characterized by unprecedented technological sophistication, while also providing unparalleled health benefits for the U.S. public. The continued benefits of genetic engineering warrant particular attention. New products generated by the biotechnology revolution cover a broad spectrum, including: genetic probes that serve as powerful diagnostics; genetically engineered drug and gene therapies; and biotechnology-based food modifications such as protein-enhanced vegetables. Increased understanding of the human genome, as well as of the genetic make-up of other organisms (genomes of other animals and plants), will yield many new and different products and applications.

The number of sources that produce these new genetically engineered products continues to escalate. The number of biotechnology firms grew dramatically from the early 1980s through 1993, so that by 1993 there were 1,272 firms, more than a threefold increase over the pre-1981 number. By April 1997, nearly 300 biotechnology drugs were in development, tripling the number that were in development in 1989. FDA must have access to the necessary scientific expertise to be able to address the complexity of these new products, and to provide sound regulatory decisions.

Microprocessor and miniaturization technologies are rapidly expanding and enabling significant improvements in implantable medical devices such as pacemakers, cochlear implants, and closed-loop medicine delivery systems that monitor conditions within the body and administer treatments as required. Progress in artificial intelligence has increased companies' ability to apply pattern recognition techniques in such

products as Pap smear readers and neural net classifiers.

New combination products, such as food-drug and drug-device combinations, will continue to be generated through the application of biotechnology techniques. Such developments foster improved versions of products already developed and approved, as well as entirely new products. New biological-based products will require the development of new data profiles, because the data used to determine the safety of chemical-based products of the past are neither sufficient nor appropriate for predicting the safety of these new products.

Biotechnology also is being used to develop new assessment tools. More emphasis is being placed on new approaches to assess the product safety of food, dietary supplements, and health care products. These tools include bioassays to improve safety assessments of carcinogencity and to address emerging concerns of neurotoxicity, immunotoxicity, and developmental toxicity.

• Growth in Recognized Adverse Effects Associated With Product Use

New technologies have provided an explosion of innovative diagnostic and therapeutic health products. The consequences of this explosion, however, include a parallel expansion of adverse effects associated with product use. Although the benefits realized from these products still greatly outweigh the problems associated with consumption, these problems must be addressed. To illustrate, FDA received more than one-quarter million reports of suspected drug-related adverse effects in 1997, and this number of adverse reports continues to increase annually. FDA estimates that nearly one million patient injuries and deaths each year are associated with the improper use of FDA-regulated products. Additional injuries and deaths occur under conditions of proper use and accidental injury. For example, of the more than 70,000 injury reports related to medical devices received annually, approximately 25 to 40 percent of the injury or death reports may be attributed to device misuse or operator error. Injury reports received by FDA only represent between 1 and 10 percent of all injuries associated with the use of medical devices. Using these figures, as many as 400,000 incidents per year resulting in patient injury or death may, at least in some way, be attributed to the user-device interaction.

Currently, the FDA Center for Food Safety and Applied Nutrition (CFSAN) receives reporting on food additives, cosmetics, and special nutritionals from the field offices and other sources. To achieve efficiency in monitoring and responding to adverse events, the Center is proposing the establishment of an integrated adverse event reporting system for food and cosmetic products. As the Agency develops more comprehensive adverse event reporting systems, particularly in collaboration with other institutions, the number of reported adverse events likely will increase. If surveillance capability does not expand, the magnitude and severity of product use problems will, to a large extent, remain unknown, and the health risks will be unaddressed.

• Unpredictable, New Health and Safety Threats

FDA continues to face a range of threats to public health that appear in a random and discontinuous pattern. For example, crippling infectious diseases such as tuberculosis are reemerging, bovine spongiform encephalopathy (BSE) became epidemic in the United Kingdom and was unexpectedly linked to the human disease, Creutzfeld-Jakob disease (nvCJD), and more virulent and antibiotic-resistant bacteria have been discovered in food products around the world. These unpredictable threats, coupled with the growing incidence of disease-causing organisms' resistance to existing drug therapies, challenge both industry and FDA to bring innovative, safe, and effective treatments to the market rapidly. The Agency also must address crises that require emergency responses, whether they are the discovery of pesticides in selected imported products, *Escherichia coli* outbreaks, or intentional product tampering. These events are byproducts of several factors, including continually expanding global trade; new entrants into domestic industries—particularly where emerging technologies are present; and economic pressures on regulated firms to reduce costs in order to ensure short-term survival.

The unpredictable nature of a significant portion of FDA's compliance activity also acts as a severe limitation to fulfilling statutory mandates of inspectional coverage. FDA is attempting to augment its inspection capability with strategies that call for collaboration with states, use of third parties to verify industry compliance, and augmenting industry quality control mechanisms. But even these augmentation strategies require front-end investments to develop systemic capabilities such as data validation, data sharing, and auditing to determine whether protocols are in place. In addition, some stakeholders oppose other third-party involvement. Consequently, in the short run FDA—even in conjunction with collaborators—will not be able simultaneously to satisfy statutory inspection requirements and address all current health and safety threats.

• More Targeted Needs and Awareness of U.S. Citizens-stakeholders

A more knowledgeable and diverse consumer population is escalating expectations for more information, as well as information that is more tailored to their particular needs, concerning the safety of FDA-regulated products. American consumers have become more health-conscious during the 1990s and are seeking more information on the impact of medical products and food on their health. FDA must distinguish between the risks perceived by consumers and their actual risks, and respond accordingly. Based on the additional information that FDA provides, consumers are playing a larger role in protecting their own health.

The elderly population provides a good illustration of why FDA must target its information and regulatory policies to fit the needs of particular market segments. Although the elderly are by no means the only segment with special needs, their numbers have become much more prominent in the general population. By the year 2000, Americans aged 75 and older will be the fastest growing group. The elderly (those over 65) have disproportionately high health care demands. Challenges associated with this patient subpopulation, such as multiple drug interactions, different physiological characterizations and reactions to drug regimens, and the need for better medical device design for home self-diagnostics and therapies, will become more acute. These challenges will require greater inclusion of the elderly in clinical testing for drugs, medical devices, and other FDA-regulated products. Further, the increasing educational needs of the elderly will require more focused education programs, including specific dietary information and foods targeted to their nutritional requirements. The elderly population and food service workers who prepare food for the elderly also will require special education initiatives concerning proper food handling, because as the population ages it becomes more susceptible to foodborne diseases.

• Emerging Regulatory Challenges in the International Arena

FDA participates in the world community of developed, underdeveloped, and developing economies and regulatory authorities. Radical changes in the dynamics of the world structure are underway, driven by several forces: (1) an increasing number of global and multinational firms that produce FDA-regulated products; (2) increasing sophistication of unified economic, political, and regional entities (e.g., the European Union [EU] and Pacific Rim countries); and (3) the response to these conditions on the part of regulatory/standard-setting entities.

The larger drug, biological, device and food firms now operate as multinational companies. New products will be developed, produced, and marketed through a highly networked and global commercial system. The system will have great power to satisfy consumer needs, but will be much more complex to monitor for potential risk than has been the case in the past. This situation will require sophisticated international regulatory responses. Further, the regulatory response by U.S. interests must preserve the delicate balance at the international level between preventing unnecessarily high-risk products from entry into the country, while providing access to novel, important therapies or foods to the American public.

The multinational and global firms are sharing center stage with an increasingly organized set of regional economic and political entities such as the EU, Pacific Rim organizations, North America Free Trade Act (NAFTA) participants, etc. These entities are amassing the economic and political power to attract world trade. The pace of their development is often uneven, but the longer term direction is clear. Raw materials and joint ventures that stretch across national borders are all becoming international elements for FDA to regulate where previously these were purely domestic phenomena. The Agency must now make new decisions on how (or if) to manage each of these new elements. Increasingly, FDA must take into account the global trade implications of its decisions.

Organizations such as the International Committee on Harmonization (ICH), the International Standards Organization (ISO), the Global Harmonization Task Force, the International Cooperation on Harmonization of Technical Requirements of Registration for Veterinary Medicinal Products (VICH), and Codex are becoming increasingly important in the determination of the level of acceptable product safety, quality, and efficacy for products trading in the international arena. FDA must maintain a viable voice as standards are prepared and speak with a voice that represents the interests of all of its stakeholders, whether they are consumers, patients, health practitioners, or the regulated industry.

• Increased Volume and Diversity of Imports

Imported products regulated by FDA represent a significant component of total U.S. consumption. In some sectors, such as seafood, the percentage of total consumption represented by imports is approximately 50 percent. FDA's responsibilities in the import arena continue to expand, without a corresponding increase in resources to do the job. To illustrate: The volume of imports has grown steadily over the past few decades. By 1998 an estimated 4 million FDA-regulated import line items arrived in the U.S. The number of food items, representing the majority of those imports, increased by 21 percent over the last year alone! During that same period, FDA resources to address imports remained essentially level.

And the complexity is increasing—the reality of a truly global economy is adding significant regulatory challenges for FDA. These products are originating in countries that often have less developed health/safety regulatory structures. The increase in volume, variety, and sources of imports may be accompanied by increases in novel pathogens, microbial contamination, and other public health concerns and regulatory challenges for FDA. Developing countries, which once provided raw materials for U.S. manufacturers, and assemblers are increasingly providing finished products to the U.S. market. This conversion could increase the risks associated with such products.

• Federal Budget Constraints

Recent budget proposals and appropriations acts have addressed emerging public health issues (such as AIDS) and long-standing public health problems that received insufficient attention in the past (including reducing youth tobacco use, improving food safety, and accelerating prescription drug approvals). While those problems continue to need attention, inflation has reduced real resources available for FDA's other public health responsibilities, which are necessary to meet the obligations delineated in FDAMA. These include inspections to ensure product safety; review of devices, food additives, blood products, animal drugs, and generic drugs; and adverse event reporting and followup.

Analysis of the Gap Between What is Expected of FDA and Its Actual Performance

FDA faces a critical issue today. Because of a convergence of challenges outlined in previous sections, the Agency has been unable to fully meet its explicit statutory obligations; nor has it been able to completely guarantee the more implicit health and safety responsibilities the statute requires and the public demands. Figure 2 illustrates that a sizable gap still exists between statutory requirements of ''on-time review'' for several product areas, and what FDA currently is able to deliver. Figure 3 shows a similar gap between mandated and actual inspectional coverage for FDA-regulated industries.

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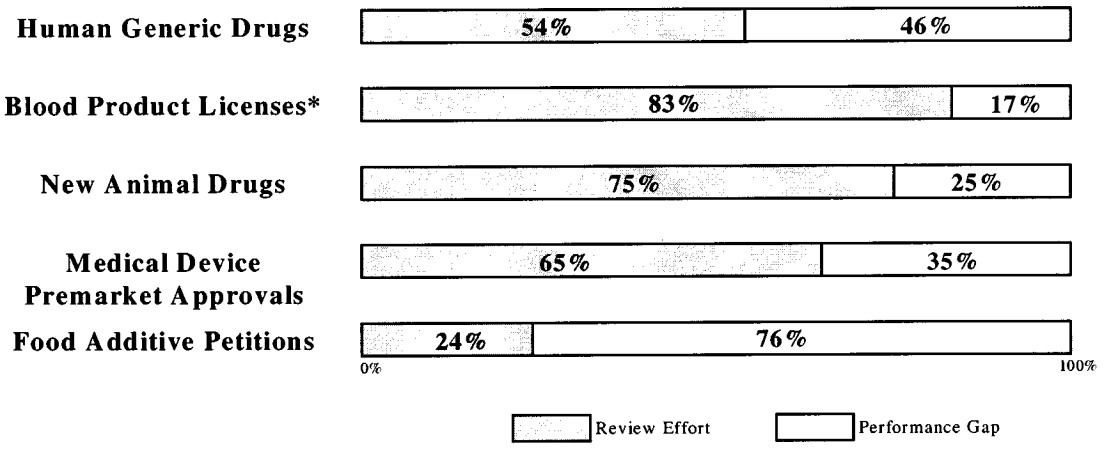
Figure 2: New Product Review Performance Gaps

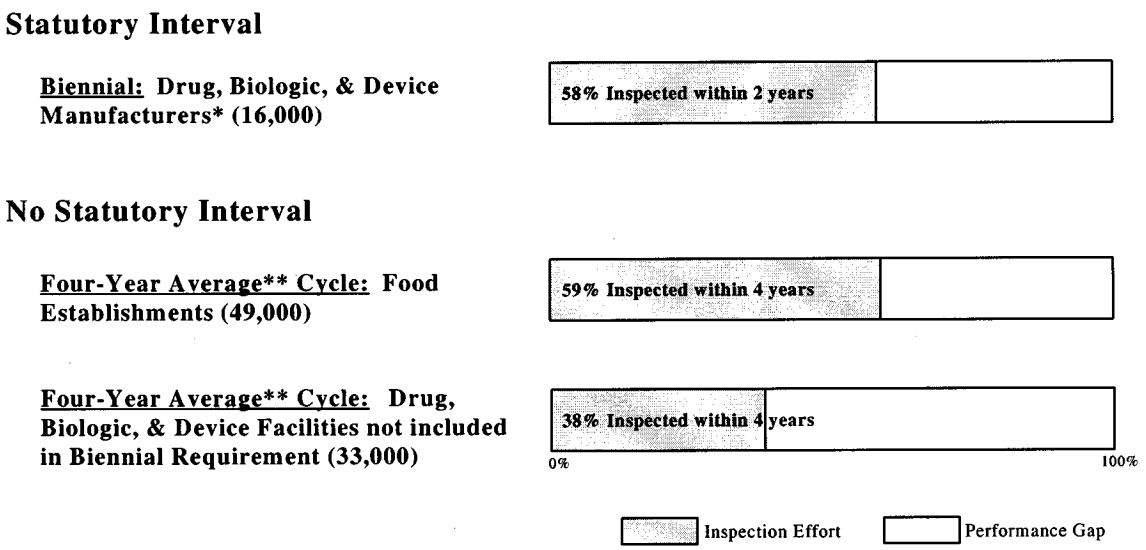
(Percentage of FY 1997 Reviews within Statutory Time Frames)



* There is no statutory requirement. FDA has adopted an internal 12-month time frame.

Figure 3: Inspection Performance Gaps

(FY 1999 Projected Inspection Effort and Remaining Performance Gap)



* Statutory requirement includes manufacturers, processors, repackers, and relabelers.

** Selected high-risk categories inspected more frequently.

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The agency has listened carefully to its stakeholders over the past several months and has combined their views with its own emerging strategies to develop a plan for narrowing the gap. The following section provides a summary of stakeholder views.

Stakeholder Consultation

FDA's assessment of the challenges it faces in fulfilling its mission and the identification of the disparity between expectations and what is achievable given the current climate set the stage for consultations with its external stakeholders. This consultation is necessary to determine the most effective ways of narrowing the gap. FDA depends on the views of its stakeholders for two crucial reasons:

(1) stakeholders are affected by the outcomes of FDA's strategies and should therefore play a role in formulating them; and

(2) stakeholders are also the collaborators that are necessary for successful implementation of the Plan.

In the sections that follow, the process of stakeholder consultation is discussed, and a summary of their views is provided.

The Process

Section 406(b) of FDAMA prescribes that the plan for statutory compliance be developed:

after consultation with appropriate scientific and academic experts, health care professionals, representatives of patient and advocacy groups, and the regulated industry.

The experts and representatives referenced in Section 406(b) comprise the constituency of the FDA. The Agency informally consults with these constituents on a regular basis. Section 406(b) codifies this process and provides a mechanism for formal input from and feedback to its constituency.

In response to this requirement, the Agency designed a process that provided multiple avenues for input, including the following:

- Public meetings were held and tailored to address concerns associated with each of FDA's product centers: foods, human drugs, animal drugs, biologics, and medical devices. In addition, there was a meeting focusing on health professionals and an Agency-wide meeting addressing cross-cutting issues.
- Dockets were provided for stakeholders to make additional comments subsequent to the public meetings. These dockets will remain open indefinitely.
- Electronic communication vehicles were established that allow stakeholders to communicate with FDA via Internet responses to the Agency's home page as well as through e-mail.
- District Consumer Forums were held to solicit comments from stakeholders.
- On going communication vehicles were used to actively solicit stakeholder views on current and future directions for the Agency. These vehicles include speeches made by the Agency's senior leadership, ongoing exchanges in smaller forums such as workshops, and one-on-one conversations.

FDA adopted a uniform approach in framing the stakeholder discussions and comments. Agency officials first outlined the stakeholder consultation process. The leadership then provided a framework outlining the emerging technological and public health challenges faced by FDA. Finally, to focus stakeholder comments and discussion, questions (Appendix B) were developed that related to each of the six objectives addressed by the 406(b) plan and were available to stakeholders prior to the meetings.

The process of engaging the Agency's stakeholders and receiving useful feedback is an ongoing one. This initial round of stakeholder views will continue to be analyzed and interpreted during Fall 1998. Results of the analysis will be shared with FDA's external as well as internal audiences. The next round of formal stakeholder meetings is being scheduled for Spring 1999, and regular contacts will continue to be maintained. Although longer term assessment is forthcoming, a preliminary evaluation of stakeholder views has been conducted. An overview of these views is provided in the next section. Stakeholder comments are assessed in greater detail in Part Two of the Plan and are related to Agency strategies.

Summary of Stakeholder Viewpoints

FDA's stakeholders commented on many aspects of the Agency's operations. The recommendations made by stakeholders regarding the Agency's priorities and the strategies FDA should use in carrying out its responsibilities reflect a wide range of concerns and perspectives. The full context of stakeholder views expressed at public meetings and in written comments are captured in transcripts and dockets that are available on FDA's Internet Web page *http://www.fda.gov/oc/fdama/comm*. Appendix B–4 also provides a compendium of stakeholder recommendations, classified both by 406(b) objectives and by the strategic directions that are identified in the next section of the Plan. Major themes that emerged from the stakeholder comments are summarized below.

Areas of Consensus

Most stakeholders agree on several broad issues. Many agreed that FDA priorities should be risk-based, scientifically rational, and focused on protecting public health. In addition, the Agency should view meeting its statutory obligations as a high priority. A number of organizations cautioned that the Agency should limit its participation in new activities, especially those that go beyond the scope of its core statutory requirements. Although stakeholders varied in their interpretations of core responsibilities, some stakeholders highlighted the importance of preserving FDA's regulatory role and encouraged the Agency to develop more creative strategies to exercise its regulatory responsibilities. Many stakeholders acknowledged the difficulties inherent in making trade-offs among program activities when resources are constrained.

Making new safe and effective treatments available to patients in a timely manner is also a high priority for FDA. To optimize the performance of the premarket review and approval system, stakeholders recommended that FDA continue to re-engineer its systems and strive for internal efficiencies; communicate earlier in the premarket review process, more frequently, and more openly with industry and other stakeholders; and make FDA policies and procedures more consistent and more transparent to industry and the public. Several groups would like FDA to adopt a more uniform and consistent approach to addressing risks of public health significance. Consistency of FDA policies and procedures seemed to be a greater concern than their transparency.

Requests for improved communication emphasized two-way communication—not only from the FDA to its stakeholders but also from stakeholders to FDA beyond adverse event reporting. Stakeholders value FDA developing a strong scientific and analytic base for its regulatory decisions. They believe that FDA should use the expertise of other organizations to help meet its goals. For example, delegating or collaborating on certain functions (such as research, standard-setting, and some aspects of product review) to third parties were offered as a means of leveraging limited resources.

Several stakeholder groups want to be more involved in FDA advisory committees. These views are consistent with FDA's transition to a more open and collaborative relationship with its

regulatory counterparts and industry. Continued FDA leadership and participation in the international arena was encouraged to ensure that international standards and guidelines are consistent with U.S. requirements. Even through it was recognized that FDA had limited resources to meet all of its statutory obligations and to meet public expectations, industry representatives opposed the collection of user fees for medical devices and the blood banking industry, as well as for veterinary products, as a means of funding premarket review activities. Similarly the concept of an ''FDA seal'', viewed as a form of user fees, was not supported.

- Areas of divergence

Although the first order of concern of all stakeholders is consumer health protection and availability of medical products, there is no consensus on the role FDA should play nor what approach should be taken in this daunting task. Key differences among stakeholders include the following:

FDA's Role in Education

Stakeholders differed sharply in their opinions on the legitimacy and primacy of FDA's role in consumer education. While some stakeholder groups believe that industry and health professionals should be responsible for consumer education, others assert that FDA should play an essential role in providing objective information about regulated products to consumers and in facilitating patient participation in ongoing clinical trials of promising new therapies. One consumer advocacy group, the National Council on Patient Information and Education, requested FDA's support in developing a collaborative, national consumer

FDA's Enforcement Activities

Some stakeholders called for expanded FDA authority and additional resource appropriations to allow the Agency to carry out its responsibilities, for example, in the areas of drug safety monitoring and monitoring the sale of unapproved veterinary products. Other stakeholders acknowledged that FDA would need to share enforcement responsibilities with others. For example, one group supported a division of tasks in the inspection arena, with FDA covering the imports, and states being responsible for domestic inspections.

Use of Third Parties

There were mixed views in this area as well. Many consumers preferred that FDA regulate the industry more directly, while several industry representatives advocated for greater use of third parties, as long as the arrangement was carefully monitored by the Agency.

Advisory Committees

Views regarding the composition of FDA advisory committees diverged greatly. Some pressed for broader presentation of interested persons while others advocated that FDA place greater emphasis on the depth of knowledge of advisory committee members. The Agency was urged to recruit renowned experts to serve on advisory committees. Some advisory committees were criticized for favoring nonscientific issues over sciences when they make recommendations.

- Unresolved Issues

Perhaps the issue that remains most problematic is the overall question of balance among FDA's functions. The appropriate mix of premarket review, post-market inspection, and surveillance activity is an ongoing topic of debate among the Agency's stakeholders. One stakeholder summed up the issue:

''How should FDA balance the need for strong and timely premarket review programs with the need for effective postmarket inspection, surveillance, and enforcement programs? That is like asking the American people to find a balance between building safe aircraft and providing adequate maintenance over the course of a plane's life.'' (Patient Group)

Although stakeholders expressed their views regarding the emphasis FDA should place on various issues, these comments frequently focused on a single FDA Center or two Competing issues. FDA does not have sufficient information at this time about the priority Agency stakeholders wish to assign to a particular issue relative to other issues competing for resources within an FDA Center or within the Agency as a whole. In some instances the proposed strategies appear to be contradictory. For example, how should the Agency balance setting risk-based priorities or meeting public expectations when doing so directly competes with meeting its statutory obligations?

Identification of Agency-Wide Objectives and Strategic Directions

The six objectives specified in FDAMA Section 406(b) and outlined on page 1 of this Plan, provide FDA with a broad framework for meeting its statutory requirements and public expectations. The Agency's senior leadership believes the following strategic directions are necessary to focus its efforts in achieving the objectives set forth by Congress. These directions represent an amalgam of approaches that have been emerging for several years, and which have been modified both by new FDA challenges and by the productive suggestions made by external stakeholders. Figure 4 identifies the link between key stakeholder themes and the strategic directions outlined in this section of the plan.

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Figure 4: FDA's Strategic Directions

• *Themes from Stakeholders*

Establish Risk-Based Priorities
- *Setting priorities*

Adopt a Systems Rather than Piecemeal Approach to Agency Regulation
- *Importance of an international strategy*
- *Adverse Event Reporting*
- *Focus inspections on systems deficiencies*

Work more Closely with External Stakeholders
- *Need for transparent FDA policies and procedures*
- *More open and communicative FDA*

Re-engineer FDA Processes
- *Need for some management reform*
- *FDA should be more creative—while maintaining control*

Strengthen the Scientific and Analytical Basis for Regulatory Decisions
- *The value of strong scientific base*
- *Strengthen the science base within FDA advisory committees and keep science base current*
- *Need for adequately trained/qualified FDA Staff*

Capitalize on Information Technology

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The strategic directions are *broad* in scope and cross-cut components of the organization. As such, they provide a context to guide all of the Agency's more specific goals and programs. They also serve as a way to galvanize diverse activities into a set of unified directions for the long-term.

(1) Establish risk-Based Priorities

Although the importance of setting risk-based priorities was a concept repeatedly endorsed by many stakeholder groups, there was not consensus regarding what constituted the highest risk areas. FDA must listen to its stakeholder community, but then it must decide, based on continuing consultation with its stakeholders, which health and safety risks most directly threaten the well-being of U.S. consumers, and allocate its resources accordingly. In the harsh light of limited resources, FDA simply cannot meet everyone's demands and cannot address all risks with the same degree of urgency or intensity. For example, the Agency is unable to respond to its highest priority health risks and at the same time fully meet its biennial statutory inspection requirements for drugs, biologics, and medical devices. it may be appropriate to reassess the practicality of mandates that emphasize industry coverage, regardless of risk, when those mandates may divert limited resources away from addressing serious health and safety concerns. The Agency has and will continue to increase the efficiency of ''fast track'' processes to address the most urgent needs for therapies so that these therapies can enter the marketplace rapidly. Resources will continue to be redirected toward the review of these products. Surveillance and compliance efforts also will continue to be directed toward identifying and taking action to correct the most serious health and safety problems associated with products that are in the marketplace or about to enter the market. The Presidential Food Safety Initiative will continue to focus attention and devote resources to those areas of the food supply that pose the greatest risk of illness and/or death to consumers.

(2) Strengthen the Scientific and Analytical Basis for Regulatory Decisions

A strong science base continues to underpin each of the Agency's regulatory decisions. Such decisions must be made throughout the lifespan of FDA-regulated products from initial research, development and testing, through production, marketing and consumption. A strong science base consists of the expertise, the risk assessment protocols, the test methods, product guidance and performance standards, and the facilities and equipment necessary for conducting excellent science. The emerging emphasis in this strategic area is to seek means for achieving synergies in science capability through access to and collaborative efforts with sources of scientific expertise beyond FDA. A recent example that the Agency hopes will achieve research synergies through collaboration is the pharmaceutical quality and drug development science initiative that the Agency has begun to pursue under a cooperative research agreement among FDA, professional societies, and industry. The initiative will provide a venue to conduct research on pressing questions about pharmaceutical manufacturing that can inform regulatory decisions regarding needs in such areas as supplement submission requirements or bioequivalence studies after there are manufacturing changes. Such collaborative efforts are reinforced in the objectives identified in FDAMA Section 406(b). The key lies in ''ensuring access to the expertise,'' wherever it is most cost-effective.

(3) Work More Closely With External Stakeholders

FDA will need to multiply the Agency's capability to address complex public health problems by working with stakeholders in planning, implementing, and evaluating solutions to these problems. The solutions don't lie solely in expanding the mass of the Agency. Consumers, the regulated industry, health professionals, and FDA's regulatory counterparts in the U.S. and abroad each represent components of a total network that can potentially improve health outcomes. To help ''activate'' that network, FDA is engaged in several strategies some just emerging and others in a more mature phase. These ''activation strategies'' include: collaboration with stakeholders to create synergies in protecting the public health; ensuring that stakeholders are well informed about the Agency's regulatory processes [the processes should be as transparent as possible] and the products that are affected by these processes; involving stakeholders early in the Agency's processes; and ensuring that all affected stakeholder groups' interests are well represented in product testing and approval decisions.

FDA is striving to create synergies through collaboration with appropriate outside colleagues in product research and testing, development, production, marketing, and consumption/use to ensure safety, quality, and efficacy.The Agency's Joint Institute for Food Safety and Applied Nutrition [JIFSAN] (with the University of Maryland) and the Moffett Center in Illinois are illustrative of such synergies working at the level of applied research and development to ensure safe foods.

Industry representatives and health professionals made it clear to FDA during the stakeholder consultation process that they can be more effective colleagues in improving health outcomes in their role as product developers and users if they are (1) well informed about the Agency's regulatory review, surveillance, and compliance processes; and (2) consulted prior to regulatory decisions on both the pre- and post-market side of product commercialization. FDA will continue implementing strategies to engage in preventive problem solving, as well as initiatives that will make the Agency's processes as clear and understandable as possible to participants.

Consumers and patients expressed a need to have prompt, complete, understandable, and unbiased information about products that FDA regulates, particularly new therapies. Well-informed consumers are more effective contributors to the management of their own health risks. FDA has launched several initiatives that are intended to keep the consumer well-informed through such vehicles as publishing the availability of important new drugs on the Internet. FDA is also attempting to ensure that the interests of all affected patients are well represented in such areas as clinical trial designs for new therapies. In addition, FDA will ensure that the interests of the consumer are represented in such deliberative bodies as advisory committees when recommendations on new products are being considered.

(4) Re-Engineer FDA Processes

FDA has used both an internal and an external focus in redesigning many of its regulatory review processes. From the external perspective, FDA is implementing several protocols that will result in simplified regulatory approaches and, as a result, a reduced burden for the regulated industry. Many of these regulatory reinventions are embodied in provisions in FDAMA. For example, the Agency may start review of a ''fast-track'' drug application before the application is complete if preliminary clinical data demonstrate that the product may be effective. Fast-track status also is being established for humanitarian medical devices, and new product development protocols will allow medical device sponsors to use

recognized study results that have been generated by other sources as part of their own application submission. Other regulatory simplification strategies have been instituted independent of FDAMA. For example, a phased review process for animal drugs has been designed that enables the Agency to provide periodic feedback to product sponsors throughout the drug review process to foster ''continuous improvement'' in the application.

FDA is also focusing internally to achieve greater efficiencies and effectiveness in its review and tracking processes. For example, implementation of project management techniques allows an opportunity for convergent thinking and action to occur so that multiple disciplines can coordinate their efforts in providing thorough but timely reviews of product sponsors' applications.

(5) Adopt a Systems Rather Than a Piecemeal Approach to Agency Regulation

Several stakeholders during the public meetings noted that they could be more efficient and effective participants in promoting and protecting public health if they could understand the total context of what the Agency was trying to do and what its future directions were. The establishment of a systems approach within FDA is closely related to the establishment of risk-based priorities. Use of a systems orientation is an effective way to identify what is truly high-priority risk and then to address that risk in a systemic manner. Systems solutions, such as the Food Safety Initiative, the integrated adverse event reporting initiative, and the important monitoring system, are examples of FDA acting in concert with other collaborators to address the highest priority, most pervasive risks facing consumers.

The Agency also has adopted a systems orientation in many of its individual programs. To illustrate, medical device inspectors have embarked on a new approach to determine industry compliance with Good Manufacturing Practices (GMPs). They are pilot-testing a systems-oriented inspectional strategy whereby medical device plants are given guidance on the establishment of a total Device Quality System, so that the control of product safety and quality is owned by the firm, rather than their having to respond to a series of external compliance requirements that must be responded to one at a time. The seafood Hazard Analysis and Critical Control Points (HACCP) initiative provides another example where FDA worked with the seafood industry to implement a systems approach to ensure the safety of seafood consumed by the American public.

(6) Capitalize on Information Technology

FDA has been on a long course of improvement in taking advantage of the opportunities offered by a rapidly evolving information technology environment. Information technology has been used for quite some time by the Agency in order to improve internal efficiencies. For example, a key element in accelerating the review of new drug therapies has been automating major portions of the drug review process. When both product sponsor and Agency reviewer can use electronic communication to establish a common ground of understanding, then all parties benefit. It is a critical element that has become pervasive in all mission-oriented as well as support activities.

More recently, the Agency has turned its attention to using information technology as a way of improving communication with external stakeholders. One of the most powerful examples of how stakeholders are assisted is in the rapid provision of information on new drug therapies via the Internet to consumers and patients. FDA's home page provides an opportunity for all of FDA stakeholders to be aware of recent Agency regulatory decisions, and, just as important, to receive input in the form of suggestions and other opinions from Agency officials. The Agency will expand use of information technology to bring relevant information to bear in the area of produce surveillance and adverse event reporting. Well-designed and integrated information systems will dramatically reduce the gap between adverse effects associated with consumption and problem correction.

Making the Transition From Strategic Context to Targeted Planning

The strategic directions outlined above provide the context for understanding Part Two of the 406(b) Plan. In Part Two, specific performance targets and associated strategies re outlined for FY 1999. Part Two is organized into sections that correspond to the six objectives outlined in Section 406(b) of FDAMA (Section 903(f) of the FD&C Act as amended). Thus, specific performance targets can be directly related to achieving the objectives of the Act.

Within each objective, strategies for FY 1999 relfect the Agency- wide strategic directions identified in Part One. Thus, the Agency's targeted planning for FY 1999 is strategically aligned with its intended directions over the next several years.

Part Two—FDAMA Plan For FY 1999

This Plan outlines key performance goals and strategies designed to achieve these goals during FY 1999. The Plan serves several purposes:

(1) It provides a blueprint for narrowing the gap between what FDA is expected to do by law and by the stakeholder community and what FDA currently can accomplish given its existing Agency resources.

(2) It responds to Section 406(b) of FDAMA, which requires the Agency to develop such a plan:

> ''The Secretary, after consultation with appropriate scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry, shall develop and publish in the Federal Register a plan bringing the Secretary into compliance with each of the obligations of the Secretary under this Act.''

(3) It moves FDA closer to fulfilling its strategic goals, and thus, its mission of consumer health protection and promotion.

(4) Finally, the Plan provides a specific set of performance commitments that will serve as a basis for managing towards results and for reporting progress.

The Plan is organized according to the six objectives outlined in Section 406(b) of FDAMA.

These objectives address critical components of FDA's responsibilities. The Agency, working in collaboration with key players in both the public and private sector, will pursue each objective as part of a total consumer health protection and enhancement system. The process begins with the research and development of new products with great health- and life-sustaining potential, and ends with the safe and effective consumption of these products. Figure 5 illustrates how FDAMA objectives are crucial elements of FDAs total contribution to beneficial public health outcomes.

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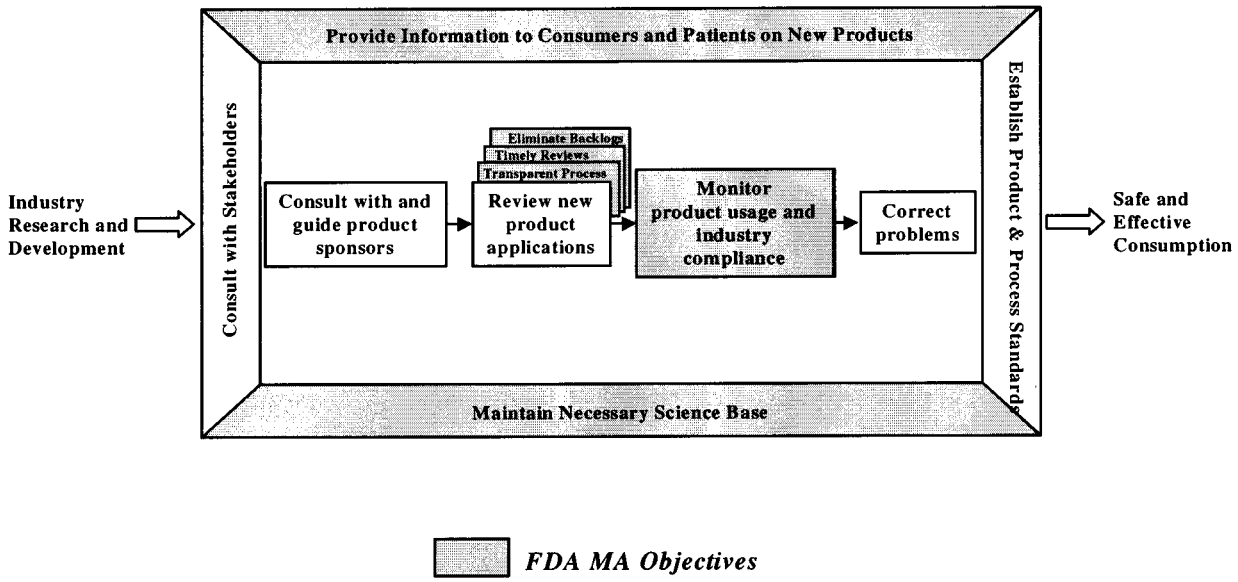
Figure 5: How FDAMA Objectives Support FDA's Responsibilities



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The six 406(b) objectives are addressed in five sections below. The five sections examine the FDAMA objectives in order by objective (A, B, C, D, and E&F). Each section provides:

- Identification of Needs—Outlines the unmet demands stated by law and expressed by the Agency's stakeholders, which FDA must address to achieve the FDAMA objective and to fulfill its mission.
- Stakeholder Views—Selected Stakeholder opinions on the importance of the need being addressed.
- Current Innovations and Reinventions—Creative improvements FDA has underway that will help achieve objectives.
- Plan for Meeting Statutory Requirements and Public Expectations—Key strategies that are planned for the future that will narrow the gap between expectations and current capabilities.
- Performance Goals for FY 1999—FY 1999 goals are based on final Congressional appropriations and may be subject to adjustment pending Agency resource allocation decisions.

Objective A—Maximizing the Availability and Clarity of Information About the Process for Review of Applications and Submissions (Including Petitions, Notifications, and any Other Similar Forms of Requests) Made Under This Act

1. Identification of Needs

FDA's ability to provide clear, adequate, and timely information on its application review processes must be improved by making FDA processes transparent to stakeholders and involving stakeholders early in the review process.

Make FDA Processes Transparent

While the Agency has developed written information (i.e., regulations, guidance documents, or internal procedures) on its review processes and requirements, more needs to be done to ensure that stakeholders understand FDA requirements. This lack of understanding is reflected in the quality of regulatory submissions received by FDA. Transparent processes also include openness on how FDA develops its requirements and how those requirements are applied within the agency during the review process.

Collaborate with Stakeholders Early in the Regulatory Decisionmaking Processes

In passing FDAMA, the Congress expected major improvements on how products are reviewed and approved by FDA. To meet this expectation, FDA must change how it responds to the product applicants during the review process—from being reactive to proactive through early applicant consultations. By consultation with product sponsors, the Agency will be able to help define the critical issues that must be addressed in a product application, to define the types of clinical trials that appear necessary, and to avoid unnecessary effort. This shifting of resources is not, however, without cost, and additional resources will be needed to meet the increasing number of product submissions generated by the doubling of biomedical research funding at the National Institutes of Health and by the regulated industry.

2. Stakeholder Views

Stakeholders endorsed the concept of a more open and collaborative relationship between FDA and its regulatory colleagues and industry. Many stakeholders commended FDA for the efforts the Agency has already made to address this objective. Requests for improved communication about application review processes emphasized not only communication from FDA to industry, but also greater stakeholder participation in regulatory decisionmaking. The examples below illustrate some of the further improvements stakeholders requested:

- Make FDA policies and procedures more transparent, particularly those related to Good Review Practices [trade association].
- Provide requested clear, concise, and up-to-date guidance to product sponsors. Where the existing guidance is deemed inadequate or scientifically outdated, FDA should issue guidance about the specific product applications [trade association].
- Work closely with product sponsors to ensure submissions are properly formatted [trade association].
- Provide a sample submission guide to applicants and make available more templates, prototypes, and examples of submissions to clarify FDA's expectations of the regulated industry and to expedite the review process [trade association].
- Provide as much feedback to industry as possible in the earliest time frame because many of the questions that are generated will result in long-term experiments or clinical trials [industry representative].
- Industry input in developing guidance documents, such as the one on inclusion of women in clinical trials, and regulations is key in maintaining the integrity of the clinical trials process and of the application review process [consumer advocacy group].
- Collaborate and interact more with the regulated industries to avoid issuing guidance documents that do not adequately take into account useful perspectives that can be provided by industry to the FDA [trade association].
- Use the formal binding presubmission consultations to reduce backlogs and to speed the approval process. [trade association].
- ''Expedite the approval of appropriate nutrient content claim and health claim petitions and citizen petitions related to food labeling.'' [trade association].

3. Current Innovations/Reinventions

FDA is improving its review processes and specific product applications through collaborative agreements, process re-engineering, and information technology.

Agreements Among FDA, Industry, and Others Enhance Review Processes

FDA, academia, and industry are working to establish a program to provide research to inform and assist FDA in developing regulations and guidance regarding the types of product quality information that should be submitted in a product application (e.g., Collaboration for Drug Development Improvement and Product Quality Research Initiative).

FDA collaborates with regulatory authorities of Europe and Japan on drug development requirements (e.g., International Harmonization).

FDA Continues to Improve Review Processes Through Process Re-engineering

FDA's medical device program improved by providing manufacturers with regulatory options to reduce regulatory burden for lower risk products and by improving communication with manufacturers. As part of the Reinventing Government Initiative (REGO), FDA has simplified the filing process by consolidating review application forms for biotechnology-based drugs, blood, vaccines, and other drugs into just one form. This enables companies to provide higher quality submissions to the FDA and reduces their application preparation time.

During FY 1997 and early FY 1998, the Foods Program conducted under contract a review of deficiencies in over 600 industry-submitted food and color additive petitions. CFSAN currently is reviewing the contractor's report and expects to use the information to improve guidance to petitions and to

implement a stronger refusal to file policy.

FDA Uses Information Technology To Improve Access of Review Processes

The FDA website (*www.fda.gov*) provides specific information to particular stakeholder groups: consumer, industry, state and local officials, patients, health professionals, women, and children.

FDA has published information on its review processes to assist applicants. For example, the FDA Center for Drug Evaluation and Research (CDER) Handbook is available on the Internet.

The Foods Program is completing testing on a document management and workflow system that will replace the current tracking system for petition reviews and will make petition data available on demand in electronic format on reviewer's and administrator's desktops. The new workflow tracking system will permit realtime access to detailed information on petition status and tasks.

4. Plan for Meeting Statutory Requirements and Public Expectations

Section 903 of the FD&C Act, as amended by FDAMA, authorizes the Commissioner to conduct educational and public information programs relating to the responsibilities of FDA. Under FDAMA (Section 406), FDA's mission is expanded to include the prompt review of clinical research and regulatory submissions, harmonization of regulatory requirements with other countries, and consultation of various experts in fulfilling the mission.

FDA's plan for meeting these statutory requirements will encompass a variety of actions intended to make Agency processes transparent and to improve collaboration between product sponsors and the agency. These include:

- Continuation of developing appropriate regulations, guidance documents, and internal operating policies and procedures.
- Expansion of the use of communication media and information technology (e.g., the FDA website) to provide written materials and information on FDA regulatory review processes.
- Improvement of the efficiency and effectiveness of Agency review processes through process re-engineering, project management, performance management, and electronic technology.
- Development of innovative approaches to facilitate sponsor and Agency consultations.

5. Performance Goals for FY 1999

The table provided in this section links the performance goals and measures with statutory requirements addressing information about the review processes. Under the FD&C Act, the Commissioner is authorized to conduct educational and public information programs relating to FDA's responsibilities. These performance goals illustrate two types of efforts. The first type identifies the development of a method that can be applied to a review process. An example would be to recognize a standard used for a medical device review. The second type identifies an improvement to enhance the Agency's ability to provide updated information or to achieve greater capability and capacity for accepting electronic regulatory submissions.

Highlighted below are key performance goals for FY 1999 in the area of electronic regulatory submissions. These goals are critical to the Agency's ability to provide timely review of clinical research and regulatory submissions, which is the intent of FDAMA. For more complete identification of performance goals and statutory requirements see the table at the end of this section.

FY 1999 Performance Goals

Complete the development of industry guidance required for electronic submission by the end of FY 2002.

Achieve electronic submission capability for certificates to foreign governments.

Achieve capability and capacity for electronic submission and archiving of information required to submit New Drug Applications (NDAs) without paper copy by the end of FY 2002.

Achieve capability and capacity for electronic submission and archiving of Abbreviated New Drug Applications (ANDAs) by the end of FY 2002.

Statutory authority	Relevant statute and/or regulation	Relevant FY 1999 performance goals	FY 1997 performance baseline
Applicants are invited to meet with FDA before submitting an application to discuss the presentation and format of supporting information. If the applicant and FDA agree, the applicant may submit tabulations of patient data and case report forms in a form other than hard copy, for example, on microfiche or computer tapes.	FD&C Act, Section 505 and 21 Code of Federal Regulations (CFR) 314.50(f)(4).	By the end of FY 2002, CDER will complete development of industry guidance required for electronic submission.	In FY 1997, electronic signature guidance was published.
Before 30 days after the date of submission of an application to export a drug, the FDA must review the application to determine if it meets all applicable requirements.	FD&C Act, Section 801(e) and 802, 21 *CFR* 210, Drug Export Amendments Act of 1986 (PL. 99–660), FDA Export Reform & Enhancement Act of 1996.	By the end of FY 1999, CDER will achieve electronic submission capability for certificates to foreign governments.	In FY 1998, develop and pilot Export Certificate Program.
For records submitted to the Agency, persons may use electronic records in lieu of paper records or electronic signatures in lieu of traditional signatures, in whole or in part, provided that certain requirements are met.	FD&C Act, Sections 201–903; PHS Act Section 3512, 21 *CFR* 11.	By the end of FY 2002, CDER will achieve capability and capacity for electronic submission and archiving of information required to submit NDAs without paper copy.	By FY 1997, establish the structure of the Electronic Document Room (EDR).
		By the end of FY 2002, CDER will achieve capability and capacity for electronic submission and archiving of ANDAs.	By FY 1997, establish the structure of EDR.

Statutory authority	Relevant statute and/or regulation	Relevant FY 1999 performance goals	FY 1997 performance baseline
Any record of the FDA that is disclosed in an authorized manner to any member of the public is available for disclosure to all members of the public, except that data and information subject to the exemptions established in 21 CFR 20.61 for trade secrets and confidential commercial or financial information, and in Section 20.63 for person privacy, shall be disclosed only to the persons for the protection of whom these exemptions exist.	FD&C Act, Sections 201–903, 5 United States Code 552, 21 *CFR 20*.	By the end of FY 2002, CDER will make publicly releasable information available via Internet.	By FY 1998, the Electronic Document Room, as required by the Electronic Freedom of Information Act, will be initiated.
Publish regulations for adequate and well-controlled clinical trials by 4/9/98 and substantial evidence by 10/9/98.	Animal Drug Availability Act (ADAA), (P.L. 104–250) Section 2(e).	FDA Center for Veterinary Medicine (CVM) will revise Investigational New Animal Drug Application procedural regulations and implement provisions of the ADAA and CVM's REGO initiatives.	ADAA enacted by 10/9/96
Recognize and approve list of standards suitable for use in application review.	FD&C Act, Sections 514 (b) and (c).	FDA Center for Devices and Radiologic Health (CDRH) will recognize over 415 standards for use in application review and update the list of recognized standards.	0 recognized

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

Objective B—Maximize the Availability and Clarity of Information for Consumers and Patients Concerning New Products

1. Identification of Needs

FDA is reviewing applications for new drugs, biologics, medical devices and food additives more quickly. Dissemination of information that will enhance consumption decisions about these new products must keep pace with the products' earlier availability. The Agency would like to provide timely information to consumers and patients, however, in some instances products are reaching the market faster than FDA can inform its stakeholders. The Agency's ability to disseminate information must be enhanced by upgrading its technology, its computers, and the training of its employees to keep abreast with the latest developments in technology. FDA is under pressure from Congress, the medical community, patients, and industry to provide timely unbiased information to its stakeholder.

• Dissemination of information to consumers and patients concerning new products must keep pace with the earlier availability of products.

• The Agency is aware of the growing diversity of consumer health needs and interests. To respond to this diversity, FDA is attempting to target product information that it is tailored, as much as possible, to appropriate patient and professional audiences.

• The growth in health benefits made possible by scientific advances and new product technology is a tremendous benefit to U.S. consumers. The speed of technology development, combined with increasing product complexity, requires creative approaches in keeping everyone rapidly and accurately informed.

• FDA recognizes that consumers and patients want and deserve active input and participation in the Agency's policy and product decisions. The Agency is receiving rapid input from consumers.

• FDA considers collaborations with others in the public and private sector critical to achieving synergies in information technology. FDA has accepted the challenge of dissemination of accurate and timely information, although at times it can be daunting, particularly because of the widespread audiences the Agency serves.

• Use of the Internet has become increasingly central in FDA communication with its stakeholders. FDA must upgrade its capabilities in this area.

2. Stakeholder Views

Stakeholders strongly agree that maximizing the availability and clarity of information to consumers and patients about new FDA-regulated products is a priority. A selection of stakeholder comments is provided below:

• ''We have consistently argued that efforts to reform the Agency must build on, not dismantle, the ability of the FDA to safeguard drug products . . . As the FDA's authority has been relaxed, we feel that safety has been relaxed as well.'' [consumer advocacy group]

• ''We see the FDA . . . as a data warehouse, as an information source.'' [professional association]

• ''. . . FDA should aggressively educate patients' advocacy groups, disease-specific organizations, disease experts, and new biotech companies about FDA's function, process, and scope.'' [consumer advocacy group]

• Ensure the validity and integrity of drug information provided on the Internet. [State, local, or federal government]

• Re-evaluate [FDA's] policy on direct-to-consumer advertising. [professional association and consumer advocacy group]

• ''Do not depend upon scientists to review the direct-to-consumer advertising.'' [State, local, or federal government]

• ''Although Congress imposed this requirement, or at least asked FDA to come up with ways to maximize information about new products, our feeling on this was that this is really not

a function for FDA to promote new products. Rather, FDA's obligation would be to refer inquiries about new products, new drugs, etc. to the appropriate parties, and that might be professional societies, physicians, medical device companies, and drug companies. [trade association]

- Use plain language on product labels. [consumer]
- Make risk and safety data and statistics available to the public via the toll-free Consumer Information Line. [consumer advocacy group]
- Inform the public when companies have been asked to revise or pull ads, and explain why. [consumer advocacy group]

3. Current Innovations/Reinventions

FDA is currently expanding its information for consumers and patients. The following are illustrations of the information exchange:

Collaboration

The Agency is collaborating with industry to inform patients and consumers of the availability of new drugs (prescription and over-the-counter [OTC] drugs). FDA engages in cooperative research with industry for new food items as well as collaborates with industry to bring better food labels and information to its stakeholders.

The Agency is collaborating with industry to provide technical, non-financial assistance to manufacturers to enable them to bring their products that meet FDA standards to the market more quickly.

Outreach

FDA has an outreach program to keep physicians informed of new drugs available to their patients. The Agency is working cooperatively with the drug industry, consumers, and patients to inform them of new drugs and emerging new drugs. Patients are able to receive information on new therapies approved by foreign countries before they are approved by the Agency. Additionally, the Agency's Public Affairs Specialists in the field offices furnish information to interested consumers and patients concerning new drugs, devices, etc.

FDA delivers educational and technical assistance in the area of food safety messages and uses. The FDA Consumer/Fact Sheets and National Food Safety Hotlines are part of the Agency's outreach. The Internet is used to bring new information to consumers and patients. Each Center has its own web page. Many of these pages are interactive and allow the user to communicate with the Agency directly. Printed materials are provided to those that are without Internet capabilities, and many of the materials are in several languages. These materials help to inform consumers and patients about new drugs. The Veterinary Newsletter, exhibits, and Public Affairs Specialists programs keep the veterinary community abreast of the newest drugs and technology being developed.

During the 20th century, the nation has witnessed a more dramatic extension of longevity than humankind has ever seen. The Agency is making a concerted effort to ensure that older persons, their families, and their communities are aware of FDA's responsibilities and how the Agency can be a resource for them in improving the quality of their lives.

FDA's consumer protection and public health mission plays a particularly important role in building a sound health foundation for ensuring quality of a long life for older persons. The needs of the U.S. aging population are stimulating innovative research and technological advancements for both preventing and treating disease. The Agency makes a meaningful contribution to this research by facilitating the timely availability of safe and effective products, keeping unsafe or ineffective products off the market, and providing easily understandable and meaningful information about the availability of new products, as well as how to use products safely and effectively. In October 1998, the United Nations launched the International Year of the Older Person 1999 to bring global attention to the phenomenon of an aging world and the need to begin to establish the policies, programs, and services needed to meet the needs of an aging world. The Agency is an active participant in this initiative.

4. Plan for Meeting Statutory Requirements and Public Expectations

Section 406(b) requires the Agency to maximize the availability and clarity of information for consumers and patients concerning new products. FDA is engaged in a variety of activities to fulfill this requirement that revolve around four themes. First are Agency efforts to ensure that product information is tailored to meet the special needs of diverse populations. One example is the implementation of public awareness campaigns for consumers, i.e., *Take Time to Care, Office of Women's Health; Mammography Awareness Seminars; Food Safety Programs (Fight BAC!™); Over the Counter Labeling Changes (OTC) Campaign;* and the *Partnership for Food Safety Education.* As the population becomes more culturally diverse, FDA must reach out to consumers in ways they will understand. For instance, Public Affairs Specialists give seminars on new drug therapies, health fraud, labeling, etc. in different languages to fulfill the needs of diverse populations.

The Agency is entering into an increasing number of stakeholder ''collaborations'' to achieve a multiplier effect (e.g., with print media, radio, television, industry, other federal agencies, consumers, health professionals, and associations). Another example is implementation of the Pharmacist Education Outreach Program to assist pharmacists in explaining the drug approval process to consumers.

Another approach is focusing FDA resources so that patients are an integral part of the health care decisionmaking process. FDA has established programs to make promising investigational drugs, therapies, and devices available to patients with serious and life-threatening conditions. For example, FDA has also included patient representatives on advisory committees considering products for HIV/AIDS, cancer, and other serious diseases.

The technological revolution provides the Agency the tools to offer quick access to a wide range of information to consumers through various methods. The Internet is being used as a means for two-way communication—both to disseminate information about new products and to quickly answer questions about new and existing products. Additionally, the Agency will participate with NIH in the establishment of (under Section 402 of the Public Health Service Act) a registry of publicly and privately funded clinical trials for experimental drugs and biologics being tested for serious or life-threatening medical conditions. This registry will simplify the process of obtaining information.

5. Performance Goals for FY 1999

The table provided in this section links the performance goals and the measures with statutory requirements to regulate information provided to consumers and to ensure that consumers understand OTC drug information. The FY 1999 performance goals focus on both OTC and prescription drugs. FDA wants consumers and patients to receive and to be able to refer to the highest quality information when taking either OTC or prescription medications.

Highlighted below are key performance goals for FY 1999. These goals seek to provide drug information, in easily understood language, to consumers and patients faster through various outreach efforts. For more complete identification of performance goals and statutory requirements see the table at the end of this section.

FY 1999 Performance Goals

Evaluate drug information provided to 75 percent of individuals receiving new prescriptions.

Improve OTC information and consumers' ability to understand it by 2001.

BILLING CODE 4160–01–M

Statutory Authority	Relevant Statute and/or Regulation	Relevant FY 1999 Performance Goals	FY 1997 Performance Baseline	FY 1998 Performance Baseline
FDA regulates prescription drug advertising and labeling by monitoring all prescription drug promotions, enforcing the laws and regulations, developing new guidance, and conducting research to support the program.	FD&C Act Sections 502(n) and 505 and 21 *CFR* 200-202	FDA will a) evaluate the availability, quality, and usefulness of prescription drug information provided to 75 percent of individuals receiving new prescriptions; and b) complete two studies that will aid in development of comprehensive drug information.	In 1996, 65 percent of patients received written information about prescription drugs. Assessments are underway to determine the degree to which this information meets the criteria for "useful" information.	Initiate partnerships with three major organizations
				Target 25 percent of review documents processed using Electronic Data Management System (EDMS)
FDA is responsible for assuring that OTC drugs are safe and effective for use—this includes improving the legibility and clarity of all OTC drug labels as well as consumer's ability to comprehend important warnings and usage directions.	FD&C Act Section 502 and 21 *CFR* 201, 21 *CFR* 211.132	By the end of FY 2001, CDER will improve the legibility and clarity of OTC drug labels, improve the consumer's ability to read and understand important warnings and usage directions; and complete two studies that will aid in development of comprehensive drug information.	*Federal Register* publication on February 27, 1997 (62 FR 9024) published a proposal providing for standardized format for labeling. Study topics have been identified and studies are being designated.	

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

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Objective C—Implementing Inspection and Postmarket Monitoring Provisions of this Act

A central part of FDA's responsibilities to protect the public health includes: (1) ensuring that manufacturing establishments and the products being produced by these establishments—both domestic and imported—are meeting safety and quality standards that are acceptable to the U.S. and (2) monitoring these products to identify and correct any problems associated with their consumption and use. Through inspection and monitoring activities, potential hazards are identified and corrected in time to prevent or minimize public exposure.

The discussion that follows is divided into these two areas of postmarket responsibility.

Subobjective C1.—Assuring Product Safety

A. Domestic Inspections

1. Identification of Needs

FDA is responsible for ensuring the safety of products produced and distributed by more than 100,000 domestic establishments. The Agency uses its inspection authority, as directed by the statute, to provide this assurance. Approximately 45,000 of these establishments manufacture or process regulated product. FDA inspected 30 percent of these facilities in FY 1997. A sizable number of the remaining establishments (23,000) are distribution facilities, of which FDA inspected 10 percent in FY 1997. The remainder includes 10,000 mammography facilities, which FDA inspects at a nearly annual rate, and a varied assortment of other establishment types, e.g. control laboratories, importer/brokers, clinical investigators, and conveyances, of which FDA inspected about 14 percent in FY 1997. Overall, approximately 40 percent of FDA's current inspectional coverage is provided through contracts with states.

As these varying inspectional coverage statistics indicate, FDA exercises considerable discretion regarding the frequency and comprehensiveness of inspections. For approximately 25 percent of this inventory, however, the law requires FDA to conduct inspections at specified maximum time intervals. Certain manufacturing facilities must be inspected at least once every 2 years, and mammography facilities must be inspected at least once each year. In recent years, inspection coverage has fallen short of meeting these statutory requirements. The table below summarizes the Agency's recent coverage of the domestic inventory including the segment subject to statutory minimum inspection coverage as well as the segment over which the Agency has discretion regarding inspection frequency. To meet the statutory requirements, 100 percent of the mammography facilities and at least 50 percent of the other statutory establishments should have been inspected in FY 1997. As the data show, with the exception of mammography facilities, neither goal was reached.

Program area	Inventory	Statutory coverage		Non-statutory coverage	
		Establishments *	Coverage in FY 1997 (percent)	Establishments *	Coverage in FY 1997 (percent)
Biologics	5,685	2,787	46	2,898	13
Human Drugs	19,749	6,408	23	13,341	12
Devices (excluding mammography)	27,638	4,870	28	22,768	9
Mammography	10,000	10,000	96	.....	.....
Foods	49,000	NA	NA	49,000	23
Animal Drugs and Feeds	6,414	1,688	27	4,726	13

* Status as of May 1998.

2. Stakeholder Views

Agency stakeholders expressed strong support for more regulatory enforcement in general, and the continued focus on risk-based inspections in particular.

- ''Stratify the inspections based upon past history of compliance of companies, the degree of risk of the product, and various other elements.'' [trade association].
- FDA should increase its efforts to monitor the marketplace to remove unapproved products and also those that provide unfair competition. [trade association]
- Inspections should take a comprehensive approach and ''focus on the health impact of the regulations, not just the 'black-and-white' of the regulations. [state, local or Federal government]
- There should be more enforcement efforts to prevent distribution of illegally marketed and compounded drugs, unapproved drugs not manufactured in accordance with current GMPs, illegal extralabel use practices, illegal distribution of veterinary prescription drugs, marketing of unapproved feed ingredients, and extraordinary claims on animal feed labels. [trade and professional associations]
- Stakeholders endorsed HACCP systems for seafood and retail settings and the possible expansion of HACCP into other food-related areas, but only when supported by science and a high consumer safety priority. [trade association]
- ''Move towards a voluntary HACCP-based system for dairy products and away from checklist inspections and prescriptive plant processing regulations.'' [trade association]
- HACCP would be applicable in general for ''foods with a demonstrated high risk (e.g., unpasteurized juice).'' In contrast, stakeholders urged the Agency not to ''promote the HACCP process for device conformance,'' but to consider ISO certifications [standard setting organization].
- Stakeholders encouraged FDA to work closely with the states and to ''be a leader (i.e., leadership in science, setting standards, evaluating state programs, certifying inspectors).'' [state, local or federal government].
- The Agency should provide more guidance and training to state investigators to minimize inconsistency between investigations in different states and districts, thereby contributing to a level playing field for regulated firms. The Agency should involve states in the development of enforcement strategies related to animal drugs and feeds. [state, local or federal government]

Stakeholders tended to support the idea of third-party inspections, especially noncritical inspections.

- The Agency should identify more functions that could be performed by third parties. [trade association]
- In some cases, particularly the manufacture of animal feeds, voluntary self-inspection with third-party oversight might be appropriate. [state, local or federal government]
- At the same time, however, the Agency needs to be careful to avoid duplication of effort and to ensure consistency between FDA inspectors and third parties. [trade association]

3. Current Innovations/Reinventions

The Agency's domestic inspection program is an integral part of the strategy for monitoring the compliance status of the regulated industry. The goals of an inspection may be many and varied, i.e., to verify data submitted to the FDA in a new drug or biologic application, and to ensure continued compliance with application commitments. Inspections monitor the regulatory control over manufacturing operations including compliance with current GMP regulations. The results of inspections form the basis for many of the Agency's administrative and regulatory decisions, including new drug, device, or biologic approvals, as well as detecting industry problems or objectionable conditions and practices.

Establish Risk-Based Priorities

Given the large inventory of establishments it must inspect with limited resources, FDA targets the highest risk products and those facilities whose violations of standards would most likely expose the public to unnecessary risk. The cornerstone of the Agency's drug (human and animal), medicated feed, biological, and medical device inspection strategy is the biennial inspection requirement, which mandates the inspection of critical establishments in the Agency's inventory, primarily manufacturers, at least once every 2 years. While FDA has no such legal mandate for food inspections, it is moving toward establishing a vertically integrated food safety system that is risk-based and which would allow it to inspect high-risk establishments every 1 to 2 years and moderate-to-low risk establishments every 4 years.

Adopt a System Rather Than a Piecemeal Approach to Agency Regulation

Manufacturing processes are becoming more complex due to the rapid advancement of science and technology. This trend continues to accelerate. This increasing complexity is mirrored in FDA's approach to ensuring comprehensive, consistent, and fair inspections.Where, in the past, the Agency often perceived its role as providing quality control for the industries it regulated, today, it recognizes the essential role that establishments themselves must play to ensure product quality assurance.The Agency is focusing more on ensuring that the systems the industry has in place to monitor the quality of its products are adequate. This approach stresses the importance of HACCP-type inspections and frequently requires that the Agency take a multidisciplined, team approach to inspections.

- the FDA Center for Biologics Evaluation and Research (CBER), which used to conduct many inspections on its own, joined with the FDA Office of Regulatory Affairs (ORA) to form 'Team Biologics' whereby teams of CBER product specialists and specially trained investigators from ORA's field force work together to conduct surveillance inspections. Follow-up compliance actions are handled under a streamlined system that provides concurrent review by CBER and ORA.
- CDER, to ensure inspection consistency, is developing standards for investigator training and certification for performance of pharmaceutical inspections.
- CFSAN has developed and implemented HACCP controls for seafood and has proposed HACCP controls for the juice industry. All seafood processors had been inspected by the end of FY 1998 to verify proper use of HACCP, and 6,681 industry officials and federal and state inspectors have been trained in seafood HACCP through the Seafood Alliance.
- CDRH, whose quality systems regulations ask manufacturers to take more responsibility for assuring the quality of devices, is moving toward systems-oriented inspections and developing HACCP-type programs for firms with a good compliance history.

Work More Closely With External Stakeholders

The Agency increasingly has emphasized communication and education as alternatives that are at times preferable to and more effective in achieving and maintaining compliance than the more traditional enforcement approaches used in isolation. It accomplishes this by providing training and workshops for industry groups, seeking the views of stakeholders, and sharing information with stakeholders and colleagues. Some examples of the Agency working closely with external stakeholders include:

- CBER produced a satellite broadcast on blood establishment inspections to educate the industry and held a workshop for manufacturers of licensed *in vitro* diagnostics.
- CDRH undertook education efforts on quality systems requirements.
- CFSAN issued guidance on GMPs and Good Agricultural Practices (GAPs), worked with the U.S. Department of Agriculture (USDA) to achieve adoption of the Food code by an increasing number of states, collaborated with JIFSAN/World Health Organization (WHO) for risk assessment, and cooperated with USDA and the Centers for Disease Control and Prevention (CDC) to implement a national education program on retail food preparation practices.
- CDER, ORA, and a major industry scientific trade organization in conjunction with a university developed a new approach for training field investigators in pharmaceutical manufacturing operations and the application of GMP and other FDA regulations to new drug development.
- CVM, in cooperation with stakeholder groups, sponsored satellite teleconferences concerning compliance with the BSE feed regulation and the Animal Medicinal Drug Use Clarification Act, which concerns extralabel drug use.
- District offices conduct ''grass roots'' meetings and industry exchange meetings on a variety of regulatory matters as a means of facilitating an ongoing dialogue with various constituencies.

4. Plan for Meeting Statutory Requirements and Public Expectations

Under provisions of the Food, Drug and Cosmetic Act and the Public Health Service Act, FDA is required to conduct biennial inspections of approximately 16,000 registered drug, biologic and device production facilities. Although there is no statutory requirement that mandates a particular frequency for the inspection of any food establishment, or those drug, biologic and device facilities excluded from the biennial requirement, the statute obliges the Agency to ensure the safety of regulated products within these establishments. Accordingly, goals have been set within these establishment categories to achieve an average inspection cycle of once every 4 years, with appropriate risk-based variations in this cycle where warranted.

FDA fell short of meeting its statutory biennial and annual inspection obligations by approximately 4,000

inspections in FY 1997. In an effort to improve its performance in these critical areas, FDA plans to rely increasingly on states and other third parties, both for direct help with some statutory inspections and for other important inspectional obligations, thus freeing some of FDA's own resources to cover additional statutory obligations. Because all public and private sector organizations in the future will be subject to the same resource-constrained environment, FDA may have to consider that even a highly collaborative inspectional network may not be adequate to completely meet existing statutory inspectional requirements. A strategic reassessment may be in order to determine the kinds of statutory flexibility that would be desirable to preserve the comprehensive consumer protection intent of the FD&C Act, and at the same time, allow FDA to address the most critical health and safety priorities. Some examples of Agency initiatives either planned or already underway include the following:

- Developing contracts with states and public health agencies to inspect unlicensed blood banks.
- Reinstating state contracts for medical gas inspections, oxygen bars, and emergency medical services. FDA is considering a pilot First Party Audit Program (FPAP).
- Concentrating its own resources on the highest risk devices such as cardiac implantables and relying on third parties for inspection of lower risk products.
- Continuing to develop contracts and collaborations with states for both statutory and non-statutory animal drug and feed inspections.
- Conducting joint surveillance work with CDC and USDA and working with the Association of American Feed Control Officials (AAFCO) to develop a model program for medicated feed manufacturers that includes self inspection.

Special Emphasis on Food Safety: The Agency recognizes its obligation to ensure the safety of the food supply, and the public expects food to be safe. To met this expectation, FDA needs to inspect high-risk establishments every 1 to 2 year and moderate-to-low risk establishments every 4 years. This level of inspection coverage will require an additional 4,000 to 6,000 annual inspections. FDA's own food safety assurance efforts is being integrated with a national risk-based food safety system. This will require close collaboration with USDA, CDC, the states, food manufacturers and food retailers. Key elements of the initiative are:

- Surveillance activities that enhance electronic communication with states and other agencies to permit rapid identification of and response to foodborne hazard outbreaks;
- A cooperative inspection and monitoring effort with states that focuses on high-risk firms, and emphasizes enforcement of initiatives such as FDA's BSE Feed regulation.
- Education emphasizing safe handling practices for consumers and retailers through FDA's Model Food Code; and
- Research to develop improved methods of detecting and identifying pathogens and formulating preventive interventions.

5. Performance Goals for FY 1999

This section contains two tables. The first table summarizes the Agency's domestic inspection performance goals for FY 1999. The second table links these performance goals to the statutory requirements.

FY 1999 Performance Goals

Inspect 46 percent of registered biologic firms
Inspect 23 percent of registered drug manufacturers, propagators, compounders, or processors
Inspect 28 percent of registered class II and III medical device manufacturers, propagators, compounders, or processors
Conduct 8,898 inspections of mammography facilities
Ensure that 50 percent of seafood industry operating under HACCP
Develop HACCP final rule for fruit and vegetable juices
Inspect 50 percent of registered animal drug and feed establishments

Statutory authority	Relevant statute and/or regulation	Relevant FY 1999 performance goals	FY 1997 performance baseline
Biennial GMP inspections of biologic firms (50 percent annually).	FD&C Act—Sec. 510(h)	Coverage: 46 percent	Coverage: 46 percent.
Biennial inspections of registered drug manufacturers, propagators, compounders, or processors (50 percent annually).	FD&C Act—Sec. 510(h)	Coverage: 23 percent	Coverage: 23 percent.
Biennial inspections of registered class II and III medical device manufacturers, propagators, compounders, or processors (50 percent annually).	FD&C Act—Sec. 510(h)	Coverage: 28 percent	Coverage: 28 percent.
Annual inspections of mammography facilities	PHS Act—Sec. 354	Conduct 8,898 inspections	Conduct 8,280 inspections.
General authority to inspect food, drugs, devices, or cosmetic establishments.	FD&C Act—Sec. 704	Ensure that 50 percent of seafood industry operating under HACCP. Develop the HACCP final rule for fruit and vegetable juices.	
Biennial inspections of registered animal drug and feed establishments (50 percent annually).	FD&C Act—Sec. 510(h)	Coverage: 20 percent	Coverage: 27 percent.

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

Subobjective C1—Assuring Product Safety (Continued)

B. Imports

1. Identification of Needs

Imported products pose multiple challenges to FDA. These include the sheer volume and diversity of products, the difficulty of ascertaining exactly which establishments are shipping products to the United States, and the difficulty of verifying conformity with GMPs quality systems. Each of these challenges, is described in the following paragraphs.

The Volume and Diversity of Products

FDA is responsible for ensuring the safety of nearly 4 million line entries that cross our borders annually, or over 12,000 entries per day. Imports of all products that FDA regulates have been increasing; pharmaceuticals, both finished and bulk, are increasing very

rapidly. Approximately $57 billion of FDA-regulated product was imported in 1997. The sources are diversifying and including more products from countries that are typically categorized as emerging economies, with emerging regulatory infrastructures. The products include, among others, food products that have been implicated in serious disease outbreaks in the United States, food products that could pose health threats if not processed and handled properly, over-the-counter drugs that do not require a new drug application with the Agency, as well as approved drugs, biologics, and medical devices.

Difficulty in Ascertaining Establishments Shipping to the United States

Section 417 of FDAMA [510(i) of the Act] now requires all foreign manufacturing establishments whose drug and device products are imported into the United States to register. There is, however, no universal registration requirement for producers of imported food products. Manufacturers/packers of low-acid canned food, acidified foods, and infant formula (all of which products are considered at high risk) register or list with the FDA; other food producers and processors are not required to register or list with FDA, making identification of sources of product difficult.

Difficulty of Verifying Conformity with GMPs/Quality Systems

There are two ways that typically are used to confirm that product has been produced properly—end point product testing (which for imports could be analysis of border samples) and on-site inspections. There are difficulties with both of these approaches. To date, no effective, scientifically based method has been established for general screening of foreign drug product for adherence to GMPs. Analysis of product samples is reasonably effective in assuring conformity, but the volume of trade and resource limitations preclude high rates of analysis. On-site inspections, the way of affirming conformity with good manufacturing practices/quality systems, are expensive and pose a host of logistical and practical difficulties. All foreign firms are aware that an FDA inspection is planned well in advance of the inspection, unlike the inspection of domestic establishments. Regardless of these challenges, there is consistent expectation from the Congress that FDA assure foreign product safety, and there is recurring congressional focus on FDA inspections of foreign manufacturing facilities.

2. Stakeholder Views

Stakeholders want assurances that foreign products meet the high standards expected of domestic products, and encourage FDA to conduct foreign inspections and periodic testing of product to confirm quality. Stakeholders strongly support FDA's activities in Codex and international harmonization, reflecting a desire to minimize regulatory burden while assuring that foreign produced food products are safe and therapeutic products are safe and effective. Stakeholders especially stress the importance of effective participation in Codex, because of the special place Codex holds in resolving international trade issues: the international standards that are adopted must reflect the standards and the high level of safety required in the United States. Support for pharmaceutical GMP mutual recognition agreements (MRAs) was predicated on the likelihood of there being equivalent standards as well as truly effective regulatory programs in MRA countries. The need for expanded funding support for Codex activities and for monitoring of imports was noted. A few typical comments are as follows:

Assurance that Foreign Product Meets High Standards Expected of Domestic Product

- ''Realizing this would require improved resources and budgets, it would still seem appropriate to perform periodic [foreign] quality assurance inspections and [border] laboratory analyses for identity, potency, and purity to ensure the quality of the drugs manufactured in foreign countries, do, in fact, equal ours.'' [state, local, or federal government]
- ''We do think more emphasis needs to be placed on inspections of imports for safety and purity, with the important caveat that such inspections should not constitute non-tariff trade barriers.'' [trade association]
- ''We have concerns regarding imported foods. In many cases, the hygienic requirements for production and processing of a food in the United States are more stringent than in countries with competing foods that are exported into the United States. More effort needs to be focused by CFSCAN in reducing the risk to the consuming public from the imported foods.''. [trade association]

Support for Codex Activities

- ''* * * the Codex has grown in significance as more and more of our nation's food supply is either imported or exported. Food regulatory bodies around the world, including the FDA, have begun to recognize that harmonized international standards are not just a good idea. They are essential if the country is going to compete in today's global marketplace.'' [trade association]
- ''Codex quality and safety standards are being utilized increasingly to resolve food safety disputes between nations in the World Trade Organization. Therefore, FDA must play an active role in Codex to ensure international standards and guidelines are consisent with US requirements.'' [trade association]

Support for Mutual Recongition Agreements (MRAs)

- ''CVM needs to determine whether foreign countries' requirements and systems for animal drug approvals ae equivalent to those in the United States.'' [trade association]
- ''While the MRA is attempting an honorable and desirable result, we would like to stress that the foreign countries should not only have equivalent standards but effective regulatory programs as well.'' [state, local, or federal government]

* * * but a Cautionary Note

- ''FDA needs to be a spokesperson for public health. The whole drive behind international harmonization is trade concerns * * * That may be fine from an economic standpoint, but it has nothing to do with FDA's public health mission. FDA needs to be there * * * to put public health * * * if not first, at least equal to trade concerns.'' [consumer advocacy group]
- ''* * * there is no question that we are bound by international agreements to harmonize regulatory standards in the area of food regulation * * * [T]his presents not only a threat but an opportunity because if we are going to go about harmonizing regulatory requirements, we can go up or down * * * When our current requirements may not be that high, we should raise our requirements and advocate the stronger requirements to become the international standard and a model for the U.S.''. [consumer advocacy group]

3. Current Innovations/Reinventions

FDA must ensure that the structure in place at the point of origin results in product being shipped to the United States meeting FDA requirements for safety, quality and/or therapeutic efficacy. This is a prevention-based strategy. A secondary strategy is detection based: conduct inspections of establishments shipping product to the United States, and screen product at the border for more intensive review.

Electronic screening allows conforming product to more quickly into commerce, while identifying product that may need more review at the border.

To deal with an explosively expanding workload and flat resources, FDA has directed its non-Prescription Drug User Fee Act of 1992 (non-PDUFA) foreign inspection activities toward higher risk products and is expanding PDUFA inspections to include more comprehensive inspections of facilities. More screening of product at the border is being accomplished through electronic means. And finally, analysis of product at the border is increasingly targeted toward product that is expected to pose high risk, as identified in the electronic screening. This risk-based prioritization means that many medium-risk product manufacturing facilities are not inspected, and most lower risk product facilities are not inspected.

4. Plan for Meeting Statutory Requirements and Public Expectations

With additional resources, FDA expects to strengthen the safety net that extends from the point of production in source countries through their entry into the U.S. These strategies encompass: (1) Reducing the probability that violative products will be exported to the United States; (2) Making rapid and reliable decisions on product entry at the border; and (3) Targeting violative products at the border and preventing their entry.

To reduce the probability that violative products will be exported to the United States, FDA will continue to participate in international negotiations and establishment of mutual recognition agreements with other nations. These activities will assure that products from those nations are meeting FDA standards, and will also increase the number of foreign inspections. As international regulatory agreements are negotiated among trading nations, the Agency will explore new and innovative institutional arrangements, such as a third-party certification of both imports and exports. These arrangements will have to be cost-effective, with statutory mandates, and enforce health and safety standards. To allow rapid entry of safe products, FDA continues to enhance its electronic screening process. To target violative products at the border, the Agency will maintain its ability to conduct laboratory analysis on a small percentage of products with potential problems, by increasing its sample analysis. The Agency will also enhance the electronic import entry system to provide for a broad-scope collection and analysis of information on product-country intersects that will allow development of national profiles. These profiles will provide the basis for establishing systematic risk-based priorities in examining import entries. Many of these efforts are obviously resource intensive, and linked closely with the steadily rising volume of imports.

5. Performance Goals for FY 1999

Consistent with the strategic directions noted above, FDA has established performance goals that support moving toward higher assurance of imported product safety in a time of increasing imports, as noted in the table below. The FD&C Act provides for sampling of product at import, and FDAMA modifications require the Agency to engage in activity designated to harmonize regulatory requirements with the objective of reducing the burden of regulations. Goals to support these activities address the short-term screening of imports at the border as well as longer term infrastructure development internationally, and these are noted in the table below. A more comprehensive table, illustrating legislative provisions, follows.

Associated with the immediate need at the border, the performance goals relate broadly to assuring the integrity of the screening system, such as by confirmation of the accuracy of entries and continual updating of the screening criteria and by improving the overall sampling and the targeted sampling rates at the border. Goals relating to international infrastructure development reflect ongoing commitment and heavy investment in international standard setting forums and negotiating equivalence agreements and mutual recognition agreements. Success in these realms would allow FDA to rely more on the regulatory structures in place at the point of origin of products being shipped to the United States. And finally, there are times when direct FDA inspections of foreign manufacturing sites are necessary to ensure the quality of product being shipped to the United States, and several performance goals reflect this need.

FY 1999 Performance Goals

Enhance the safety of imported products through increased surveillance of imported food products at the border, increased foreign inspections (from a target level of 40 to 75–100), through providing education, outreach, and technical assistance to foreign countries on the use of GAP/GMP guidance for produce, and through the evaluation of food production systems in foreign countries.

Enhance import screening capabilities for public health while ensuring that 55 percent of entries are released within 15 minutes.

Assess potentially violative imports through direct examination of 3 percent of entries.

Accept at least 20 percent of imports into the U.S. market through evidence that source country quality systems/standards/ audits meet the requirements of the FD&C Act.

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Statutory Authority	Relevant Statute and/or Regulation	Relevant FY 1999 Performance Goals	FY 1997 Performance Baseline
		Enhance the safety of imported products through increased surveillance of imported food products at the border, increased foreign inspections (from a target level of 40 to 75-100), through providing education, outreach, and technical assistance to foreign countries on the use of GAP/GMP guidance for produce, and through the evaluation of food production systems in foreign countries.	FY 1998: Participate in all meetings of Codex Alimentarius Committees that elaborate food safety standards including limits for contaminants in foods, codes of practice (e.g., GMPs) and guidelines (e.g., HACCP and decisions on equivalence); all World Trade Organization and NAFTA SPS matters involving food safety, discussion of all trade disputes involving legal interpretations of provisions of trade agreements that have implications in upholding U.S. food safety requirements.

Statutory Authority	Relevant Statute and/or Regulation	Relevant FY 1999 Performance Goals	FY 1997 Performance Baseline
The Secretary of the Treasury shall deliver to the Secretary of Health and Human Services, upon his request, samples of foods, drugs, devices and cosmetics which are being imported or offered for import into the United States, giving notice thereof to the owner or consignee, who may appear before the Secretary of Health and Human Services and have the right to introduce testimony...If it appears from the examination of such samples or otherwise that (1) such article has been manufactured, processed, or packed under unsanitary conditions, or in the case of a device, the methods used in, or the facilities or controls used for, the manufacture, packing, storage or installation of the device do not conform to the requirements of section 520(f) [GMPs] or (2) such article is forbidden or restricted in sale in the country in which it was produced or from which it was exported, or (3) such article is adulterated, misbranded, or in violation of section 505 [NDA provision], then such article shall be refused admission, except as provided in subsection (b) of this section [relabeling, reconditioning]...	FD&C Act 801 (a)	Enhance import screening capabilities for public health while ensuring that 55 percent of entries are released within 15 minutes	FY 1997: 50 percent
		Assess potentially violative imports through direct examination of 3 percent of entries.	FY 1996: approximately 3.3 percent FY 1997: approximately 2 percent

Statutory Authority	Relevant Statute and/or Regulation	Relevant FY 1999 Performance Goals	FY 1997 Performance Baseline
The Secretary shall support the Office of the United States Trade Representative, in consultation with the Secretary of Commerce, in meetings with representatives of other countries to discuss methods and approaches to reduce the burden of regulation and harmonize regulatory requirements if the Secretary determines that such harmonization continues consumer protections consistent with the purposes of this Act. The Secretary shall support the Office of the United States Trade Representative, in consultation with the Secretary of Commerce, in efforts to move toward the acceptance of MRAs relating to the regulation of drugs, biological products, devices, foods, food additives, and color additives, and the regulation of GMPs, between the European Union and the United States. The Secretary shall regularly participate in meetings with representatives of other foreign governments to discuss and reach agreement on methods and approaches to harmonize regulatory requirements. The Secretary shall, not later than 180 days after the date of enactment of the Food and Drug Administration Modernization Act of 1997, make public a plan that establishes a framework for achieving mutual recognition of good manufacturing practices inspections	FD&C Act 803		
		Accept at least 20 percent of imports into the U.S. market through evidence that source country quality systems/standards/audits conform to the requirements of the FD&C Act.	The international trade data used to evaluate the status of this goal are affected by the nature and timing of evolving international agreements and standards. These data will be used to determine the volume of imports that conform with FDA requirements under these agreements and standards.

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

BILLING CODE 4160–01–C

Subobjective C2—Adverse Event Reporting

1. Identification of Needs

FDA needs to work with its community of stakeholders and develop a systematic approach to address the problem of over 2 million injuries and deaths a year occurring as a result of consuming/using FDA-regulated products. The ideal approach should be comprehensive, involving the participation of regulatory agencies, health care givers, the regulated industry, and the consumers/patients themselves. Components of this system include:

- *A full understanding of the causes of product-related deaths and injuries:* FDA needs to ensure that causes attributable to product labeling, design, or composition are addressed in the premarket review programs, where required. FDA currently receives yearly thousands of reports of injuries and deaths associated with the misuse or failure of FDA-regulated products. FDA should improve the quality of information on adverse events and product failure and develop methods to enhance understanding of causes of product-related injuries. Currently, for example, the FDA's ability to identify and track the causes of food-borne illness is very limited.
- *New postmarket information-gathering programs:* FDA often has little date with which to make fundamental decisions about some products. This is especially true for products like foods and cosmetics for which no premarket approval is required. New programs must be initiated, in collaboration with other agencies, to provide such data. The Agency also needs to implement new ways of gathering data. The National Sentinel Reporting System, a nationally representative sample of medical device user-facilities, is expected to be a less expensive way of providing better and quicker data on medical device-related problems than the 100 percent mandatory reporting system now used. This system cannot be implemented without the necessary funds.
- *Rapid dissemination of findings:* FDA needs to be an active participant in a multi-institutional network that can detect adverse effects quickly and can disseminate information to health professionals industry, and consumers quickly.
- *Outreach and education:* A significant component of improving the current situation is to improve the feedback to health care personnel and consumers. Requested resources will be devoted to developing strategies , such as consumer publications and public service announcements, to reduce the number of injuries from food and cosmetic products.

2. Stakeholder Views

There is strong stakeholder support for improving the data collection, analysis, and dissemination of information from the existing Adverse Event Reporting System and for some of the news data collection initiatives. A few indications of these views follow:

- ''The process for adverse event/injury reporting is perhaps the most urgent task facing FDA today. The process by which adverse injury report data is captured and converted to agency and consumer use must be addressed.'' [consumer advocacy group]
- ''Perform analysis and trend reporting on error and accident reports and make this available to the industry.'' [trade association]
- ''Improve the handling of adverse event reports for dietary supplements to involve the industry earlier.'' [trade association]
- ''Consumer safety is being threatened by funding cuts in 1996 that eliminated the adverse-reaction report part of the voluntary reporting program for cosmetics. [trade association]
- ''Accurate food safety statistics are vital to developing an effective strategy for enhancing the safety of our nation's food supply.'' [trade association]

3. Current Innovations/Reinventions

FDA has initiated several programs for gathering information on adverse events/injuries associated with the misuse or failure of FDA-regulated medical products and foods. These include the following:

MedWatch

MedWatch covers drugs, biologics, medical and radiation-emitting devices, and special nutritional products, such as medical foods, dietary supplements, and infant formulas. The MedWatch form is used for voluntary and mandatory reporting of adverse events and product problems by health professionals; the reports are sent on to the appropriate FDA component for analysis and follow-up action. Over 140 health professional and industry organizatios have joined the MedWatch effort as MedWatch Partners and actively support the program by promoting the importance of reporting serious adverse events or product problems to their members.

Adverse Events Reporting System (AERS)

With its new computer system, the *Adverse Events Reporting System (AERS)* is expected to form the basis for a revitalized pharmacovigilance program for the United States. AERS continues to be developed and will be relied upon by both CDER and CBER over ensuring years to provide accurate, accountable data for the performance goals identified for injury reporting.

FDA is responsible for monitoring the market for adverse effects of medical devices. FDA expects to receive over 63,000 postmarket reports in FY 1998, including mandated reports from medical device manufactures; voluntary reports from medical device professionals received through the problem reporting program (MedWatch); and results of field inspections. FDA currently is managing the huge numbers of reports in three phases. During the first phase, the reports are screened for completeness and entered into the data management system. During the second phase, the reports are analyzed for similar events, judged for severity, and searched for trends. The final phase focuses on action, such as issuing safety alerts and notifications to users (i.e., health professionals and patients) warning them of concerns and advising them how to prevent future occurrences.

Some manufacturers have been granted approvals to submit summary reports quarterly for adverse events involving specific devices. This summary erporting system is bieng expanded and will produce usable information at a small cost to both FDA and the industry.

FoodNet

FoodNet is the product of a cooperative venture among USDA, CDC, and FDA; it attempts to estimate the incidence of foodborne illness that is not revealed in obvious outbreaks. Most foodborne illness occurs in ways that appear sporadic and unrelated to each other. FoodNet, which has the ability to provide more comprehensive information through sources such as case-control studies and surveys of laboratories and physicians, can help FDA and its federal colleagues link illnesses that have a common cause, no matter where they occur.

National Antimicrobial Resistance Monitoring System (NARMS)

The National Antimicrobial Resistance Monitoring System (NARMS) was established in January 1996 as a collaborative effort among the FDA, USDA, and CDC. The system was

initiated in response to public health issues associated with the approval of fluoroquinolone products for use in poultry. The NARMS program monitors changes in susceptibilities to 17 antimicrobial drugs of zoonotic enteric pathogens from human and animal clinical specimens, from healthy farm animals, and from carcasses of food-producing animals at slaughter. The objectives of the system include: to provide descriptive data on the extent and temporal trends of antimicrobial susceptibility in *Salmonella* and other enteric organisms, to facilitate the identification of resistance in humans and animals as it arises, and to provide timely information to veterinarians and physicians. The ultimate goal of these activities is to prolong the lifespan of approved drugs by promoting prudent and judicious use of antimicrobials and taking appropriate public health action.

Vaccine Adverse Events Reporting System (VAERS)

CBER and CDC jointly overseas the *Vaccine Adverse Events Reporting System (VAERS),* which receives mandatory reports as required by the National Vaccine Injury Act about adverse effects from vaccines. CBER and its colleagues are discussing electronic submission of reports, which would provide more rapid access of the VAERs data to manufacturers.

4. Plan for Meeting Statutory Requirements and Public Expectations

Prompt identification of new, previously unrecognized problems with FDA-regulated products has the potential to decrease morbidity and mortality associated with those products and maximize the safety of approved products. Thousands of deaths and injuries could possibly be avoided, or their consequences reduced, through a comprehensive strategy aimed at finding out why incidents occur and implementing strategies to prevent them from occurring again.

One of the Agency's primary objectives is the development and implementation of a system for improving the quality of information on adverse events and product defects associated with FDA-regulated products. This system needs to address issues of injury reporting by focusing on three areas: surveillance and epidemiology; research; and education and outreach. FDA believes that such a system would maximize the safety of FDA-regulated products through increased reporting of potentially dangerous adverse events or product problems to FDA or the manufacturer. Increased reporting provides greater assurance that a potential problem with a marketed product will be discovered and appropriate corrective action will be taken, and it ensures systematic feedback to the health care community and the public. None of these systemic improvements are possible without adequate funding.

Surveillance and Epidemiology

- With sufficient resources, FDA continues to develop and revitalize its system for reporting, monitoring, and evaluating adverse events associated with FDA-regulated products. AERS is the basis for this revitalized program.
- FDA is also developing active reporting systems for foods and for medical devices. These active systems use statistical selection of sites to provide better estimates of adverse events from the events that are reported.
- FDA will implement a National Sentinel Reporting System to provide an alternative to 100 percent mandatory reporting by medical device user-facilities. The system will use a nationally representative sample of user-facilities to track postmarket adverse events and is intended to save the industry millions of dollars in reporting costs. The system also will provide FDA clinicians and analysts with more timely, and better quality, postmarket data, thus improving FDA's ability to detect and to analyze medical device-related problems. In addition, this system is intended to provide FDA with ready access to a network of clinical facilities that could offer clinical insight into problem investigation and participate in specific research and educational efforts on product problems. However, this cannot be implemented without the necessary funds.

Research

Methodologic and surveillance research efforts designed to understand the causes of, and the factors contributing to, product-related injuries are critical to reducing the number of FDA-regulated product injuries. Research will be initiated in ''human factors sciences'' to identify labeling and product interface design features that may cause or contribute to use error, a leading cause of avoidable deaths and injuries.

Education and Outreach

Improving feedback to health care professionals and consumers is critical to the improvement of adverse event reporting. Rapid dissemination of findings on injuries to the relevant stakeholders and the education of the medical community require additional resources. The Agency has begun to collaborate with other agencies and professional groups to produce teleconferences that convey general information or product-specific information, nationwide.

An integrated science-based system for reporting, monitoring, and evaluating food and cosmetics-based adverse events is necessary to make fundamental regulatory decisions and policies. This system will depend on a research program aimed at understanding how health care professionals, as well as the public, can better recognize product-problems, and on a related research program on methods of analyzing the data. The clinical evaluation of adverse events and the determination of risk assessment requires medical officers and other trained personnel to take follow-up actions, make clinically-based decisions, and report activities to FDA's existing staff.

5. Performance Goals for FY 1999

The table provided in this section links FDA's statutory requirements with performance goals in the FY 1999 Performance Plan, illustrating the Agency's efforts to consolidate several systematic approaches into one performance system.

Highlighted below are key performance goals for FY 1999 in the area of adverse event reporting. These performance goals deal with creating new, active surveillance systems, or with improving passive reporting programs to make them more useful and available. For more complete identification of performance goals and statutory requirements see the table at the end of this section.

FY 1999 Performance Goals

Implement AERS for the electronic receipt and review of Adverse Drug Report (ADR) reports

Evaluate pilot efforts for new postmarket surveillance system

Increase the number of reports on device events that are received and processed in summary form by using electronic reporting

Develop baseline surveillance data on foodborne illness under the FootNet program

Improve public access to information on adverse events with Special Nutritionals

Increase the number of human and animal isolates in National Antimicrobial Resistance Monitoring System (NARMS)

Statutory authority	Relevant statute and/or regulation	Relevant FY 1999 performance goals	FY 1997 performance baseline	FY 1998 performance baseline
Applicants must report to FDA adverse drug experience information.	FD&C Act, Section 505; Public Health Service Act, Section 2101–2134; 21 *CFR* 314.50, 314.80–81, 314.98, 314.540, and 600.80.	By the end of FY 1999, implement the AERS for the electronic receipt and review of voluntary and mandatory ADR reports.	Implementing the core system is currently under way and will be completed by FY 1998.	FY 1998: Pilot, five firms electronic entry uncoded only. Periodic reports only.
Plan and implement a sentinel user reporting system.	FD&C Act Section 519(b)(5).	Evaluate pilot efforts for new sentinel device reporting system as alternative to universal user facility reporting.	Not applicable	Recruit 24 pilot facilities.
CDRH				
Device user-facilities are required to report adverse events.	FD&C Act Section 519(b)(1).	Increase the number of low-risk postmarket reports received and processed in summary form. The total number of summary reports will be increased from 20,000 in FY 98 to over 25,000 in FY 99. This will be done by using innovative surveillance methods and improving quality and analysis needed for Safety Alerts and other actions..	Not applicable	FY 1998: 20,000 reports received in summary form.
CDRH				
CFSAN	.....	Work with CDC and other federal agencies to develop baseline surveillance data on foodborne illnesses required to evaluate the effectiveness of, set better priorities for, and determine appropriate outcomes for the Food Safety Initiative.	Sentinel Sites expanded to provide better coverage of the representative areas of the United States.	Expand the demographic diversity and size of the population covered by FoodNet by increasing the number active surveillance sites from 7 to 8. Begin implementation of PulseNet, which provides data required to do more rapid and accurate tracebacks to determine the causes of foodborne outbreaks.
CFSAN	.....	By the end of FY 1999, improve public access to timely information on adverse events related to dietary supplements, infant formulas, and medical foods by increasing the frequency of public releases of information in the Special Nutritionals Adverse Events Monitoring System from two per year to four per year.	Two releases in FY 1997.	The requisite hardware and software systems need to be purchased for integration of current Center-based limited capability systems.
CVM	.....	Assure that food derived from animals and animal products is safe for human consumption by increasing the number of human and animal isolates in the NARMS database.	*Salmonella* isolates: 1,287 human, 2,391 veterinary.	*Salmonella* isolates: 2,000 human, 3,000 veterinary.

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget Submission to Congress.

Objected D—Ensuring access to the scientific and technical expertise needed by the Secretary—

1. Identification of Needs

FDA's ability to access the scientific and technical expertise necessary to carry out its mission must be enhanced, i.e., improving the science infrastructure, by upgrading the status of its facilities and equipment; augmenting and targeting its science expertise toward important new health enhancing technologies; and linking its science information to external sources.

Upgrade Facilities and Equipment

FDA's current science capability, both internally generated and externally coordinated, supports a wide range of risk management activities, covering the life cycle of Agency-regulated products. The integrity of the science base should be sustained by state-of-art equipment and facilities, but at a minimum they must be in good repair. The present status of this infrastructure, in many cases, is considerably less than adequate. For instance, replacing the FDA's Los Angeles laboratory and expanding the Arkansas regional facility will provide the physical tools necessary to meet FDA's obligations.

Augment and Target Science Expertise

Although FDA's science efforts are supporting current efforts in premarket review, postmarket safety assurance, and product use monitoring, these programs are falling short of meeting the Agency's statutory mandates and public expectations. As the programs are enhanced to meet expectations, the Agency's access top state-of-the-art science must be expanded. This will be accomplished both through strategic recruitment of needed expertise *and* through creative collaboration with outside institutions. Because FDA must regulate increasingly complex products, the Agency's science capabilities must be able to keep pace with new scientific developments. Further, the science expertise must be positioned so that appropriate risk assessments can be targeted toward emerging technologies that are significant in protecting public health and which must reach the market place quickly.

Link Science Information to External Sources

FDA must make strides in linking its science information bases to external sources so that synergies can be realized and appropriate information can be brought to bear on risk assessment and risk management decisions promptly. If FDA does not enhance its ability to link its science information with other outside sources, it will lose comparability and communicability with these sources. Further, it will not be as able to capitalize on cost-effective use of science information to support regulatory decisions.

2. Stakeholder Views

Stakeholders strongly support the need for FDA maintaining a strong and well-linked science base to support increasingly complex regulatory judgments. A few illustrations of these views are indicated below:

- ''These needs to be a continuing strong commitment within the Food and Drug Administration towards maintaining an appropriate scientific base. It has been the experience of our member companies, with numerous examples relating to both clinical development and complex manufacturing issues, that these are speedily resolved because of the scientific expertise within [FDA]. [trade association]
- ''Our company's long history in biotechnology has repeatedly shown the value of active research scientists at [FDA]. [FDA's] personnel that are involved in research related to safety, efficacy, basic biology, mechanism of action, and other associated areas provide an important component for in-depth understanding of issues and bring an understanding and response to issues in a scientifically and regulatory responsible and appropriate manner.'' [industry representative]
- ''[FDA] Staff need to understand modern science . . . there is just not going to be any way that proper regulation can occur without people being able to communicate at the same level about this science. There needs to be maintenance and renewal of the state-of-the-art scientific leadership.'' [professional association]
- ''I express the public's strong interest in the Agency's ability to retain highly qualified scientists within the FDA. I ask, and adverse reporting statistics demand, that products be reviewed on the merit of scientic evidence, safety and effectiveness.'' [consumer advocacy group]
- Implement programs whereby Agency scientists participate in staff exchange programs with academia, other government agencies and industry. [health organization]

3. Current Innovations/Reinventions

FDA is expanding its access to scientific expertise through creative collaboration with the broader scientific community. This is being accomplished through several approaches:

Industry-Government-Academic Collaboration

Industry-government-academic collaboration enhances the Agency's scientific expertise, thereby using added resources that would otherwise be unavailable to the government. Examples of these collaborations are below.

- The FDA Science Board, a high-level committee of representatives from industry and academia advise the Commissioner and Chief Scientist on FDA scientific issues and activities.
- FDA has two significant collaborations with industry, the Collaboration for Drug Development Improvement (CDDI) and the Product Quality Research Initiative (PQRI), intended to leverage resources and to work with industry to improve the drug development process.
- FDA currently has approximately 25 collaborative research and development programs (CRADAs), which are designed to foster scientific collaboration between the federal government and sectors outside the government; a list of these programs can be found on the FDA Internet site. FDA is actively soliciting new collaborative agreements with industry in addition to advertising opportunities on the Internet.
- FDA has joint programs with the University of Maryland and the Illinois Institute of Technology to enhance safety of the food supply. This is particularly important in light of the government's Food Safety Initiative, which is designed to assure the American public that they can consuming the safest food possible.
- FDA annually sponsors a Science Forum and workshops to bring together scientists of like disciplines from across and outside the Agency to address cross-cutting topics. Examples of recent workshops include the deoxyribonucleic acid (DNA) microarray workshop, alternative toxicology testing methods, and mechanisms of carcinogenesis.

Intergency Collaboration

Encourage interagency cooperation allows the substantial expertise of other government scientists to focus their efforts on similar problems. For example, working with other agencies allows the FDA to prevent illness and epidemics. The Agency collaborates with the NIH to speed drug and vaccine development so these products can reach consumers more quickly. This interagency cooperation also allows the Agency to determine modes of infection and thereby educating scientists, which could lead to new testing methods.

Exchanging Scientific Expertise

Industry and FDA collaboration provides an atmosphere to encourage the exchange of scientific expertise. The FDA sponsors workshops on cutting-edge topics such as gene therapy and Simian Virus and DNA vaccines. The FDA/National Institute of Dental and Craniofacial Research (NIDCR) model MOU allows for use of scientific expertise on panels and as consultants to the CDRH's device group. Added to these face-to-face contacts, Agency scientists are encouraged to publish in professional journals so their non-government peers can learn from their work.

Information Technology

Information technology is a tool that allows FDA scientists to learn about new discoveries and to increase their abilities to review applications. For the Agency to produce excellent scientific work, FDA scientists must be aware of the latest developments and theories quickly and in a timely fashion so they can incorporate them into their work. Facing these scientists is the daunting task of accessing a voluminous amount of new information, which is generated too quickly for one person to follow. To assure this knowledge is incorporated into Agency decisions, FDA scientists use information technology to access databses of latest discoveries located in-house and in external scientific databases.

Information technology (IT) tools go beyond finding articles with new theories and approaches. The Agency uses IT tools to validate computer models to speed reviews. For instance, FDA scientists can review a comprehensive database on carcinogenicity of over 700 drugs. IT tools also are used to validate computer models in a timely manner so application decisions can meet statutory requirements.

4. Plan for Meeting Statutory Requirements and Public Expectations

Section 903 of the FD&C Act, as amended by FDAMA, requires FDA to carry out research relating to foods, drugs, cosmetics, and devices in realizing the intent of the Act. Section 903 also requires FDA to consult with experts in science, medicine, and public health and other stakeholders in carrying out its mission. In addition, FDAMA law (Section 414) mandates policies that foster collaboration between federal agencies and other science-based agencies.

FDA's plan for meeting these statutory requirements will encompass a variety of actions intended to enhance its science capabilities. One approach is for the Agency to conduct research projects that identify the causes of and factors contributing to product-related injuries. For instance, Agency scientists are examining labeling and product features that can be altered to prevent product-related accidents. To conduct these research efforts, the Agency will maintain and strengthen its in-house scientific expertise by expanding innovative and successful programs (e.g. in-house Fellows programs).

The Agency will continue to enhance its scientific collaborations with the larger scientific community by initiatives with the University of Maryland, Georgetown University, and other institutions of higher learning. Similarly FDA will strengthen the Agency's science base linkage to external sources to provide comprehensive science underpinning for important national health initiatives, such as working closely with CDC and USDA in the establishment of NARMS.

In addition to these steps, the Agency is developing improved methods to detect food pathogens and to assess health risks more rapidly so that consumers can implement preventive measures.

5. Performance Goals for FY 1999

The table below links the performance goals and measures with the science-related statutory requirements. FDA's main statute, the FD&C Act, provides broad authority to the Secretary to authorize research efforts. Performance Goals illustrate two types of efforts. The first identifies development of methods or products that can be applied to a specific health risk problem. For instance, one goal calls for studies on antibiotic resistance of foodborne pathogens.

The second type of goal identifies a long-range systemtic solution to a range of problems. Illustrative of this type is a multi-year research plan to improve methods for detection, control, and prevention of microbial contamination. A measure for this type of goal is more difficult to establish. Because scientific progress often results from diverse efforts, measuring this goal is an incremental process of small steps. In this goal, establishing relationships with stakeholders is a major step.

Highlighted below are key performance goals for FY 1999 in the area of science. Several goals enable the Agency to put science behind methods for quickly detecting potentially high-risk products. Other goals focus on collaborating with key stakeholders to increase science's role in regulatory policy. For more complete identification of performance goals and statutory requirements see the table at the end of this section.

FY 1999 Performance Goals

Implement a multi-year research plan to develop and improve methods for the detection, control, and prevention of microbial contamination on fresh produce.

Develop model to assess human exposure to a variety of foodborne pathogens.

Work with industry and academia to develop new techniques for eliminating pathogens on fresh prodcue.

Support product review by developing faster, more accurate tests on mechanisms of toxic actions.

Demonstrate a model toxicity knowledge base to support and expedite product review.

Develop better models to predict risk for cancer, reproductive, developmental, neurological, genetic, and acute toxicological outcomes.

Statutory authority	Relevant statute and/or regulation	Relevant FY 1999 performance goals	FY 1998 performance baseline
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Develop and begin implementing an inter-agency research plan that more effectively coordinates the food safety research activities in FDA and USDA.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	

Statutory authority	Relevant statute and/or regulation	Relevant FY 1999 performance goals	FY 1998 performance baseline
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Formalize PQRI collaboration.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Identify specific issues and areas of research focus and develop research protocols.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Identify priority material for standard development.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Use model animal and cell culture transgenic systems to evaluate risk to the human genome.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Conduct case-control molecular epidemiology studies to assess breast and prostate cancer in African-American women/men.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Computer-based predictive system is being used as model for rodent and human hormone-binding proteins.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Present at a scientific forum a unifying approach to safety assessment for both carcinogenic and non-carcinogenic effects.
The Secretary is empowered through the Commissioner of FDA to conduct "research relating to foods, drugs, cosmetics and devices".	FD&C Act, Section 903(d)(2)(C).	.....	Screen animal products and environments for a microorganism harboring antibiotic resistance.

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

Objective E—Establishing Mechanisms, by July 1, 1999, for Meeting the Time Periods Specified in This Act for the Review of all Applications and Submissions Described in Subparagraph A (Objective A) and Submitted After the Date of Enactment of the FDAMA

In the spring of 1999 FDA plans to reevaluate where it stands in relation to this objective. The Agency plans to make information on this objective easily available to Congress, the public, regulated industry, and other stakeholders. FDA is exploring making this information available on the Internet.

Objective F—Eliminating Backlogs in the Review of Applications and Submissions Described in Subparagraph A (Objective A), by January 1, 2000

Objectives E and F are directly related. The strategies followed to achieve Objective E will also achieve Objective F. By making improvements and changes to the review process to meet the time frames for reviewing applications and submissions, any backlogs for them will be eliminated. Therefore, this section will address both objectives.

1. Identification of Needs

While, the Prescription Drug User Fee Act of 1992 (PDUFA) has been a great success, there is a gap in performance for applications not covered by PDUFA that needs to be filled for FDA to meet its statutory review requirements. In addition, public expectations, internal time frames, and PDUFA goals provide important benchmarks for FDA performance.

FDA needs to reduce total product development time, meet statutory review requirements, expedite and add value to new technologies, maintain high-quality interactive reviews, and target laboratory work to support and expedite science-based reviews. FDA has successfully adopted a number of innovations and re-engineering approaches to improve review performance. FDA has now reached the point, however, where additional improvements toward meeting statutory requirements cannot occur without additional resources.

FDA ultimately needs to speed safe and effective products to the American public by reducing the overall development and review time for new products without compromising product quality and safety.

2. Stakeholder Views

Making new products available to the public more quickly and streamlining the product development and review process while ensuring safety are important goals.

• Some consumer advocacy groups want the Agency to assign the highest

priority to expediting the development and review of drugs, while others expressed fear that meeting review deadlines could result in safety risks.

• ''Replace the resource-intensive [Generally Recognized as Safe] GRAS petition process with a streamlined notification system. Finalize the GRAS notification regulation.'' [trade association]

Using a risk-based strategy for reassigning resources is a major Agency strategy. A number of stakeholder comments seemed to support this strategy.

• A major health organization stated that many blood products have been in the public arena for a long time, and placing such products on the lowest review requirement tier would allow the transfer of resources to new products.

• A health professional society said that FDA should reassess the risk-benefit of analysis of lifestyle-modifying drugs and subject them to a different type of scrutiny than that which is used to treat or to prevent disease or other medical conditions. Also, they said it is hard to argue that it is worth taking a lot of work with a new drug product which in no way adds therapeutic benefit.

A number of stakeholders said that proper implementation of fast-track provisions will expedite entry into the marketplace for drugs for serious and life-threatening illnesses.

• A biotechnology industry council suggested that the PDUFA II goals be applied first to fast-track products. They also said that definitions need further clarification and a broad, flexible definition is needed for ''serious and life-threatening illnesses.'' The council also suggested that quarterly conferences be held to discuss surrogate end points and that fast-track designation should be done by directors of review divisions.

There was both support for the Agency's strategy for implementing third-party reviews and also concern about the strategy.

• A major trade association said that more medical devices should be added to the list for using third-party reviews.

• A regulatory organization said that FDA should continue to offer its reviews as an alternative to third-party reviews and that FDA should carefully review the third-party evaluations just as it would the work of its own staff.

A major concern of industry stakeholders was that FDA communicate what is expected of them in developing and testing new products and in providing evidence for approval.

• A major trade association said that FDA should make its procedures transparent, particularly in terms of Good Review Practices (GRPs). Various documents such as GRPs and reviewer handbooks should be provided to industry and other stakeholders to provide a better understanding of the workings of FDA and to allow industry to bring its procedures into conformity.

Improving the efficiency of the review process by implementing an electronic submission and review process was also an industry priority.

• A biotechnology industry representative suggested that information flow and documentation needs to be handled more efficiently and suggested that this could be done through the establishment of a standard electronic information exchange environment that would set the standards for industry.

Animal drug industry stakeholders placed a high priority on FDA implementing the recently enacted Animal Drug Availability Act (ADAA).

• Full implementation of the ADAA was an issue brought up by many of the stakeholder groups, including drug manufacturers, livestock producers, and feed producers. All of the speaker who mentioned it strongly urged FDA to devote whatever resources were necessary to fully implement ADAA.

3. Current Innovations/Reinventions

FDA has been pursuing a number of strategies for many years to improve on-time performance in reviewing applications and submissions, especially for new products. Many of these strategies were developed in conjunction with the Agency's stakeholders. Many strategies focus on speeding up the review process and encompass risk-based priorities, re-engineering FDA processes, information technology, communications with industry and other stakeholders, and scientific support for reviews.

Strategies also focus on the drug development stage (i.e. pre-Investigations New Drug [pre-IND] and IND), and on assisting industry during the testing and pre-application process. A day saved in developing a new therapy is just as valuable as a day saved in reviewing it. FDA is working with product sponsors to ensure that they know what is expected of them so that product testing and preparation of the application are more effectively and efficiently done. As PDUFA has shown, these pre-application efforts have resulted in higher quality applications, faster reviews, and an increasing approval rate. Non-PDUFA applications have benefited from PDUFA improvements and innovations. However, FDA performance on non-PDUFA applications still needs improvement.

FDAMA start-up and additional workload may reduce review performance in the near term, especially for medical devices and other non-PDUFA products. The growing complexity of medical devices requires that more time be spent interacting with sponsors and keeping guidelines up to date. Increased guidance and interactions with industry are resource-intensive activities. These factors will challenge FDA's ability to meet time frames.

Establish Risk-Based Priorities

FDA is focusing more on actual and potential risks in establishing priorities. FDA will identify and concentrate resources on high-risk, high-impact products or work areas, those where its direct intervention helps consumers and health care professionals the most. Despite current and anticipated budget constraints, resources will be redirected; and while some key areas will be increased, some low-risk product areas will be decreased. Several examples of these effects include:

• Exempting low-risk medical devices from the premarket notification requirement;

• Using a threshold of regulation approach for very low risk noncarcinogenic indirect food additives.

• Giving priority to high-risk, food safety-related, food additive petitions.

Conducting risk versus benefit communications research to assess the public's ability to understand risks versus benefits in drug information and to develop useful and meaningful ways of presenting important information about a drug's known risks and benefits.

FDA's research agenda includes development of more predictive animal and non-animal models for safety and efficacy evaluation. FDA scientists are developing new approaches for use in predicting risk associated with human toxicity; developing computer-based systems to aid in the assessment of human toxicity; and conducting research on specific agents, concepts, or methods that can be applied to questions of human health and safety.

In addition to the risk-based priorities, FDA has identified high-impact areas such as pregnancy labeling, antibiotic resistance, medication errors, consumer information and direct-to-the consumer advertising policies that require the expenditure of further resources. In conjunction with stakeholders, FDA already is devising innovative strategies and methods to address the public health impact of these emerging issues.

Re-Engineer FDA Processes

The Agency has been working to change its culture to fulfill its dual mission of promoting and protecting public health. As a result, FDA has been re-engineering many of its product review processes for the last several years. In fact, many e provisions of FDAMA codified results of re-engineering efforts initiated by the Agency. The following provides highlights of a variety of re-engineering efforts, resulting from FDAMA, other laws, stakeholder input, and the Agency's own initiative.

The introduction and expansion of the Project Management System (PMS) to expedite review processes for both CDER and CBER established team-based project management programs designed to improve the quality and efficiency of the drug review process. These programs have demonstrated their effectiveness and continue to be refined and enhanced. Team-Based Project Management is a powerful technique combining the use of multidisciplinary teams led by project managers and scientific leaders who use the tools and techniques of project and resource tracking. Review disciplines are organized into multidisciplinary teams early in the review process to develop a review plan and commit to target interim and milestone completion dates. Teams meet periodically to exchange information, discuss significant aspects of the applications, review progress toward meeting target completion dates, and make resource adjustments. Project management is being used throughout the Agency.

FDA is committed to the implementation of the third-party provision of FDAMA and is already pursuing that program. A key factor will be to apply lessons earned from the earlier third-party pilot program for medical devices. The fact that the earlier pilot worked well for the limited number of manufacturers who participated in the program, combined with the expanded list of eligible devices under FDAMA, should go a long way toward attracting additional submissions from industry.

FDA plans to issue guidance that describes its fast-track policies and procedures. To ensure compliance with the legislatively managed time frame of 60 days for designation, FDA is using management tools similar to those which have contributed to FDA's success in meting PDUFA goals. The guidance will include the Agency's definition of ''a serious or life-threatening condition.'' In accordance with the statutory mandate, FDA currently is working with NIH, sponsors, and its advisory committees in the timely evaluation of proposed surrogate end points. For many years FDA has been working with sponsors to develop surrogate end points that are reasonably likely to predict clinical benefit for serious and life-threatening conditions.

Streamlining efforts will be focused on reducing the overall time required for product development. More guidance and meetings will be provided during the development process to assist firms in conducting appropriate clinical trials and in developing the scientific evidence needed to gain approval of new products.

During FY 1998 CFSAN implemented a proposed notification procedure for independent GRAS determinations. The Agency's current plan is to codify this process during FY 1999. Once codified, this procedure will largely replace the resource-intensive GRAS affirmation petition process with a less resource-intensive notification process.

Other efforts to simplify regulatory approaches and to reduce the burden on stakeholders include:

- Implementation of a phased review process as in CVM where CVM works with the sponsor throughout the research and development process and reviews technical sections of a New Animal Drug Application (NADA) as they are completed;
- Implementation of additional premarket notification programs in lieu of requiring preapproval before marketing (For example, CFSAN has worked to prepare for implementation of a premarket notification program for food contact substances established by FDAMA.);
- Development of GRPs for Agency reviewers (CBER and CDER conducted a series of workshops to develop an action plan that will evolve into guidelines that describe and develop GRPs guidance. A reviewer's handbook is also being developed.);
- Development of a list of approved drugs for which additional pediatric information may produce health benefits;
- Elimination of certain labeling requirements;
- Amendment of regulations to provide additional flexibility for health claims on foods and to clarify nutrient content claims; and
- Allowing use of abbreviated study reports in an NDA.

Capitalize on Information Technology

FDA is aggressively moving towards an electronic regulatory submissions environment. The benefits of electronic submissions include:

- lower paper handling costs for FDA (e.g. document room contract, offsite storage, onsite storage);
- quicker access to information by reviewers (e.g. no waiting for a paper copy and no rekeying of data for analysis; and
- time and cost savings during product development (most firms have their data in electronic format and won't have to waste time creating/delivering a paper submission to FDA).

Work More Closely With External Stakeholders

A common theme in all of the improvements to the review process has been an intensive effort to improve communication with sponsors and manufacturers. This dialogue, which occurs by telephone, by videoconference, and in person, helps manufacturers understand what FDA is looking for in product submissions. Explanations include what information will be needed and why. Unresolved questions are resolved on the spot. Communication with industry continues to improve, with more companies taking advantage of opportunities to consult with FDA.

These efforts have already contributed to improved review performance. For example, CDRH has zero backlogs of 510(k)s, Pre-Marketing Approvals (PMAs), and PMA supplements. In addition, CDRH has begun implementing additional meetings as required by FDAMA, such as determination meetings, where a prospective PMA applicant may request a meeting to determine the type of scientific evidence necessary for PMA approval; agreement meetings, where prior to submitting an Investigational Device Exemption (IDE) application, a sponsor may request a meeting with FDA to discuss the specific investigational plan for a class III or implantable device; and 100-day PMA meetings, where within 100 days after the submission of a PMA, the sponsor may request a meeting to discuss the application.

FDA is working to make Agency processes transparent by providing a variety of information in a variety of ways including:

- Increased sponsors/applicants meetings;
- Presubmission conferences;
- Presentations to industry about a variety of topics on the most common GMP deficiencies that prevent approval;
- Providing potential applicants with assistance during the development process;

• Comprehensive guidance for preparation of submissions to FDA; and

• Initiating industry education programs/services regarding studies and safety data needed to support petitions and notifications.

FDA continues to rely on outside advisory committees for advice in reviewing product applications. Outside experts add a wide spectrum of judgement, outlook, and state-of-the-art experience to FDA's decisionmaking process. These expert advisors add to FDA's understanding, so that final Agency decisions reflect a balanced evaluation. FDA is working to improve the advisory committee process and make-up of committees to address stakeholder concerns.

FDA participates in international harmonization activities that can result in reduced regulatory burden for the regulated industry, much of which markets products throughout the world. By harmonizing requirements to the maximum extent possible, the industry hopes to reduce the costs involved in bringing products to market. Activities are underway in the Codex Alimentarius forum to develop and adopt a standard for food additives. Activities to date have also included work toward major parts of common technical documents that could be used for premarket filings in the three major industrialized markets. Efforts are underway with medical devices to identify areas of divergence in the various regulatory requirements, with an eye toward ultimate harmonization of requirements. With drugs and biologics, these activities should result in both higher quality products regardless of production site, and their getting on the market quicker due to reduced conflict in regulatory requirements in major markets. By relying both on manufacturer self certification of conformity with international harmonized standards as part of the accepted premarket application and on third-party reviewers for preliminary 501(k) determinations, FDA has reduced the demand on staff to review original documentation.

Strengthen the Scientific and Analytical Basis for Regulatory Decisions

Addressing the adequacy of the research and scientific infrastructure is one of FDA's highest priorities, especially as it supports the review of pre-market applications. Laboratory work is targeted to develop in-house scientific expertise, scientific guidance, and science-based standards. In-house scientific expertise is used to consult on product reviews, especially in areas of emerging technologies. Guidance can benefit both applicants and review staff in developing and reviewing applications. FDAMA requires FDA to recognize and use appropriate standards in the application review process for medical devices. Evidence that a product meets established standards will expedite the review process.

FDA still faces shortages of certain expertise, especially through attrition. Some positions are very difficult to recruit. FDA needs to use a number of pay incentives (higher initial pay, bonuses, comparability allowances, etc.) to attract and retain medical officers, especially for certain specialties. Other positions include pharmacokinetics specialists, statisticians, and computer specialists. As a result, FDA sometimes is lacking critical skills in the review area such as having an orthopedic surgeon to review surgical devices.

4. Plan for Meeting Statutory Requirements and Public Expectations

Because of the success of PDUFA, FDA will continue to use PDUFA submission and review mechanisms to improve the review performance of non-PDUFA applications and reduce product development time. Ultimately matching PDUFA's success without additional resources comparable to those provided by user fees is problematic.

PDUFA is different from some European review systems in that it provides the certainty of a result within a definite time. Examples of the submission and review mechanisms used to accomplish this are: (1) presubmission consultations; (2) refuse-to-file authority and increased application quality; (3) project management; and (4) complete first actions.

Several interlocking strategies will be used to meet FDA's review goals. To ensure wise use of reviewers' time, FDA will continue to re-engineer its product review processes in many areas and will continue to look for more effective means of shortening processes without sacrificing quality and safety concerns. Second, several initiatives are underway to reduce the direct review burden on the Agency by reducing the requirement for pre-approval in some areas and replacing it with an industry notification process. Third, consultation with product sponsors early in their research and development process will raise the likihood that high-quality commercial applications will follow and make their way through the FDA system in the shortest time possible. Finally, all of FDA's product review centers will continue to automate their application submission and review tracking systems. This should result in not only faster review times, but also increases in Agency productivity. Without an infusion of resources, however, it is unlikely that FDA will be able to meet its statutory obligations in all product areas.

Additional Steps

Make available and reassign more resources by using a risk-based priority system and seek additional resources as needed. FDA will redirect resources to high-risk and high-impact product areas and decrease resources in areas that pose a lower risk or benefit.

Expand collaboration with product sponsors to expedite product development.

Provide more productive interactions with industry through up-to-date guidance review, industry education, and reviewer training.

Increase efforts with other industrialized countries to harmonize product protocols.

Expand electronic submission and review systems.

Target laboratory support for emerging technologies.

Expand use of third-party reviews.

5. Performance Goals for FY 1999

The table provided in this section highlights some key PDUFA and non-PDUFA applications and summarizes the time frames, performance goals, baseline performance, and the number of applications overdue. A more comprehensive table and listing of applications and submissions covered by this Plan are in Appendix D.

The PDUFA time frames and performance goals are the result of in-depth negotiations between the drug industry and FDA. Industry and FDA determined that both the time frames and the percentage goals were realistic, achievable with the additional user fee resources, and desirable. The PDUFA time frames for drug applications differ in some cases from the FD&C Act statutory requirements. Biologics applications are covered by the Public Health Service Act, which does not have any statutory time frames. Also, the PDUFA goals do not stipulate that 100 percent of applications be completed on time. In many cases, however, a 100 percent performance level was achieved. Industry is pleased with the certainty of a timely action and response from the review process and the net result of a higher percentage of applications being approved faster. Patients have benefitted by having more therapies available more quickly. Performance goals for PDUFA

applications are based on the PDUFA time frames.

Performance goals for non-PDUFA applications are based primarily on the statutory time frames with two exceptions. Non-PDUFA biologics applications have no time frames. FDA has voluntarily adopted the original PDUFA time frames for these applications. Also performance goals for food and color additive petitions are based on 360 days, twice the statutory time frame of 180 days. This is being done to provide realistic targets as the petition review process is being re-engineered.

FDA has developed clear performance goals that will enhance and further expedite reviews for product applications. Setting these goals has provided a valuable management tool for identifying performance expectations and assessing achievements. Using the PDUFA model, performance is measured based on the percentage of applications acted on within the appropriate review time frame. The on-time performance measure is important because it represents definitive decisions both to approve and not to approve. An accurate portrayal of the timeliness of the Agency's decision making should focus on the length of time to all decisions, both positive and negative.

Overdue applications are those whose review period exceeded the time frames and were under active review at the end of the fiscal year.

Highlighted below are key performance goals for FY 1999 in the area of application review. These goals represent applications for new and priority products and for new medical uses of approved products. For more complete information see the table at the end of this section and Appendix D.

FY 1999 Performance Goals

Review 90 percent of priority NDAs/PLAs/BLAs within 6 months.
Review 90 percent of priority efficacy supplements within 6 months.
Review 70 percent of blood PLAs/BLAs within 12 months.
Review 50 percent of PMAs within 180 days.
Review 30 percent of food and color additive petitions within 360 days.

Time frame	Relevant statute	Percentage of first actions within review time period		Overdue*
		FY 1999 performance plan goal (percent)	FY 1997 baseline (estimate) (percent)	
PDUFA:				
Review Priority NDAs within 6 months (CDER) (PDUFA II commitment letter).	FD&C Act Sec. 505(b) requirement is 6 months.	90	100	0
Review Standard NDAs within 12 months (CDER) (PDUFA II commitment letter).	FD&C Act Sec. 505(b) requirement is 6 months.	90	99	0
Review Priority NDAs/PLAs/BLAs within 6 months (CBER) (PDUFA II commitment letter).	FD&C Act Sec. 505(b) requirement is 6 months. None for PLAs/BLAs.	90	100	0
Review Standard NDAs/PLAs/BLAs within 12 months (CBER) (PDUFA II commitment letter).	FD&C Act Sec. 505(b) requirement is 6 months. None for PLAs/BLAs.	90	100	0
Review priority efficacy supplements within 6 months (CDER & CBER) (PDUFA II commitment letter).	FD&C Act Sec. 505 requirement is 6 months for NDAs. None for PLAs/BLAs.	90	100	0 (CBER)
Non-PDUFA:				
Review ANDAs within 180 days (CDER)	FD&C Act Sec. 505(j)	60	54	
Review and act on blood and source plasma PLAs/BLAs and PLA/BLA major supplements within 12 months (internal time frame) (CBER).	No statutory requirement	70	83	4
Review PMAs within 180 days (CDRH)	FD&C Act Sec. 515(d)(1)(A)	50	65	0
Review 510(k)s within 90 days of receipt	FD&C Act Sec. 510(k) and (n)	90	98	0
Review food and color additive petitions within 360 days. (CFSAN) Goals are based on 360 days. FY 1997 baseline based on 180 days**.	FD&C Act Sec. 409 and Sec. 721 requirement is 6 months.	30	**24	
Review NADAs and ANADAs within 180 days (CVM)	FD&C Act Sec. 512(c)(1)		75	

*The number of applications overdue at the end of FY 1998.

**(Within 180 days) For petitions received in FY 1996, using the previous petition review procedure, 24 percent of petitions received ''first action'' within 180 days. CFSAN re-engineered the petition review process in FY 1998 and redefined ''first action.'' FY 1997 figures and FY 1999 are not directly comparable.

FY 2000 Performance Goals are not identified in this Plan. Specification of these goals is dependent upon final determination of the President's FY 2000 Budget submission to Congress.

FDAMA Plan Appendices

Introduction

These appendices and corresponding Internet resources provide direct access to information being used within FDA to implement the FDA Modernization Act. The actual text of the law passed by Congress, verbatim comments from stakeholders related to improving the way FDA conducts business and the current implementation plan are available for review and comment.

Considerable space is devoted to stakeholder participation. Even so, only a fraction of the information is attached—the balance of information has been organized on FDA's website (*http://www.fda.gov*). By clicking on ''FDA Modernization Act'' anyone can navigate through the wealth of FDAMA-related materials currently available.

The text of the FDA Plan for Statutory Compliance is located on the Internet at <*http://www.fda.gov/oc/fdama/fdamapln/default.htm*>. Additional questions or comments or requests for printed copies of these Appendices may be directed to the Planning and Management Communications Staff by telephone at 301–827–5207, by e-mail to *schasin@oc.fda.gov*, and by FAX to 301–827–5225.

Appendix A: Statutory Authority

http://www.fda.gov/oc/fdama/fdamapln/appenda

(1) Section 903 of Federal Food, Drug, and Cosmetic Act

(2) Section 406 of FDA Modernization Act of 1997

Note: Section 406 of the FDA Modernization Act amends, and has been incorporated into, Section 903 of the Federal Food, Drug, and Cosmetic Act. Copies of both sections have been included here. They include FDA's current mission and annual reporting requirements.

Appendix B: Stakeholder Involvement in 1998

http://www.fda.gov/oc/fdama/fdamapln/appendb

(1) A message to FDA Stakeholders (includes 7 key questions)
(2) Supplemental questions asked of stakeholders
(3) Written summaries of each stakeholder meeting
(4) Stakeholder comments organized by FDAMA objectives

Note: Involving stakeholders in modernizing the way FDA meets its statutory and public health responsibilities is perhaps the most significant advancement addressed in FDAMA. In 1998 FDA made dramatic progress in gathering ideas for improving the Agency's effectiveness. Stakeholders include experts in science, medicine, and public health, as well as consumers, product manufacturers, importers, and retailers. Most of the information contained in this section is also available on FDA's website.

Appendix C: FDAMA Implementation Chart

http://www.fda.gov/oc/fdama/fdamapln/appendc

Note: This chart shows FDA's current status on implementing FDAMA. It provides a section-by-section overview including a brief description of each task, statutory deadlines, and key contacts within the Agency. This is the actual implementation framework used by the Agency.

Appendix D: Application and Submission Review

http://www.fda.gov/oc/fdama/fdamapln/appendd

Note: This report includes a summary of 32 of FDA's most important functions as they relate to applications from manufacturers. Examples of these requirements are, ''Review priority New Drug Applications within 6 months,'' and ''Review infant formula notifications within 90 days.'' Also included are statistics that show current performance levels, future targets, and overdue applications. Other applications and submissions are also identified.

Other Information Resources Available via Internet

FDA's web site at *http://www.fda.gov/oc/fdama/comm* includes a special section on the FDA Modernization Act of 1997. Various reports, meeting summaries, stakeholder comments, and implementation updates are available continuously for persons with Internet access. Visitors can learn more about FDA as well as view first-hand the Agency's progress in achieving its mission.

Full text of FDAMA, Public Law 105–115: *http://thomas.loc.gov/bass/d105/d105laws.htm1*

Transcripts of public meetings: *http://www.fda.gov/ohrms/dockets/dockets/98N0339/calendar.htm*

Federal Register Notice of 9/14/98 public meeting *http://www.fda.gov/ohrms/dockets/98fr/082098b.pdf*

FY 1999 Performance Plan *http://www.fda.gov/ope/FY99pplan/pplan.htm*

Department of Health and Human Services (DHHS) main web site: *http://www.dhhs.gov.*

Dated: November 16, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

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