

**DEPARTMENT
of HEALTH
and HUMAN
SERVICES**

**Fiscal Year
2000**

Food and Drug Administration

***FY 2000 Performance Plan
and Revised Final FY 1999
Performance Plan***

***Government Performance and Results Act of
1993***

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Note: Final FY 1999 performance goal commitments are found in [Appendix 2](#) of this document.

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Welcome to FDA's FY 2000 Annual Performance Plan

This U.S. Food and Drug Administration (FDA) Agency Performance Plan is organized into two components:

Part One outlines FDA's strategic framework that will position the Agency to meet the scientific and regulatory demands of the 21st Century. The framework consists of:

1. An enhanced mission statement that has been prescribed by the FDA Modernization Act of 1997;
2. The key environmental challenges that FDA must address if it is to carry out its mission successfully in the 21st Century;
3. The gap between expected and actual FDA performance;
4. Stakeholder viewpoints on FDA's future directions;
5. Approaches that FDA will be implementing Agency-wide to support its major strategic initiatives; and
6. Strategic initiatives that are intended to reduce the gap between what is expected of FDA and its actual performance.

Part One also includes the FY 2000 goals that FDA has identified in its role as an NPR-designated High Impact Agency.

Part Two includes both the revised final FY 1999 Performance Plan, based on final appropriations, and the FY 2000 Performance Plan.

The revised final FY 1999 Performance Plan appears as a final list of the Agency's FY 1999 performance commitments, and a summary of changes to the previously published FY 1999 goals. This information is found in Appendices 1 and 2.

The FY 2000 Performance Plan includes performance goals for FY 2000, the approaches that will be used to pursue them, and the total resources required to achieve these goals. The performance goals are grouped by FDA's programs: Foods, Human Drugs, Biologics, Medical Devices and Radiological Health, Animal Drugs and Feeds, the National Center for Toxicological Research, and Tobacco. These organizational components will be responsible for implementing the plan and achieving the goals.

PART ONE: FDA'S STRATEGIC FRAMEWORK FOR THE 21ST CENTURY

For more than 90 years, the Food and Drug Administration's primary mission has been to promote and protect the public health. FDA will continue to carry out that mission in the 21st century, but in a much more complex and rapidly changing environment. This section outlines the strategic framework by which that the Agency leaders are organizing and focusing FDA's response to these changes. The initial component of this framework is a revitalized mission statement provided by Congress as a part of the FDA Modernization Act of 1997. A key feature of the updated statement is the Agency's commitment to work closely with its stakeholders in promoting and protecting the public health.

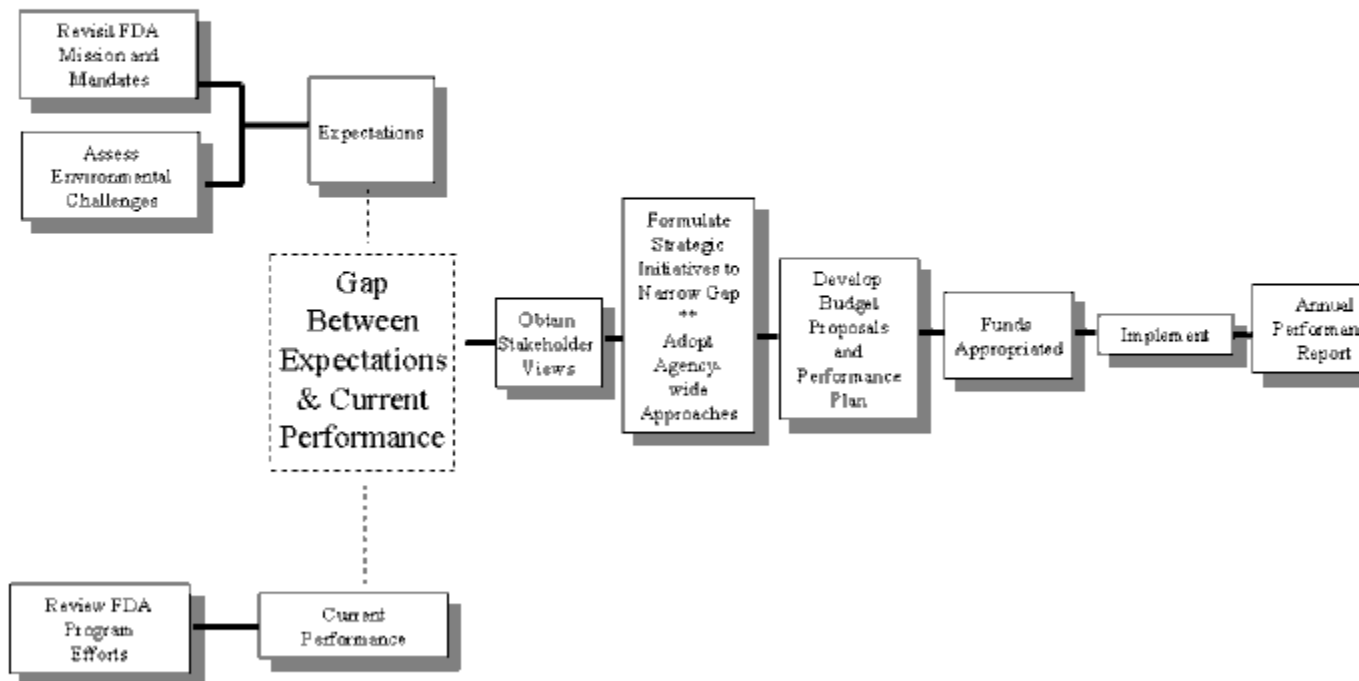
As a second key component of its strategic framework, FDA leadership has conducted an assessment of both its external and internal environments in order to identify the challenges the Agency will be facing over the next several years. This has included delineation of FDA's statutory requirements and public expectations, evaluation of environmental factors that will affect the Agency's future actions, and a review of current program performance. As a result of this assessment, leaders have identified the broad dimensions of a gap between what FDA is required and expected to accomplish and what it is currently able to achieve. During the summer of 1998, FDA leaders discussed this gap with many of its external stakeholders and received several constructive suggestions on possible future courses of action.

Based on its own assessment and the recommendations of stakeholders, FDA has formulated a plan to narrow the gap between expected and actual performance. This plan

includes broad strategic initiatives that will be pursued over the next several years, Agency-wide approaches that will be implemented to strengthen all initiatives, and annual performance plans for FY 1999 and 2000 that translate these broad initiatives into specific performance commitments. FDA, with the help of its stakeholders, will continually evaluate the effectiveness of its strategic initiatives and performance goals, and will report on its progress to Congress and other stakeholder groups. Figure 1 outlines the strategic management process that FDA implemented in developing the strategic and performance components of the Agency Performance Plan.

Figure 1

FDA's Strategic Management Process



FDA Mission

1. To 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

FDA's Revitalized Mission

With the passage of the FDA Modernization Act of 1997 (FDAMA), Congress enhanced FDA's mission in ways that recognized the Agency would be operating in a 21st century characterized by increasing technology, trade, and complexities in public health protection. To meet these challenges, Congress added explicit phrasing to the Agency's mission statement to ensure that FDA would coordinate its efforts with regulatory counterparts worldwide. In addition, Congress recognized that scientists both within and outside the Agency play critical roles in carrying out FDA's responsibilities. Finally, Congress placed new emphasis on the need for FDA to interact on a regular and meaningful basis with its stakeholders.

- public health by ensuring that foods are safe, wholesome, sanitary, and properly labeled; human and veterinary drugs are safe and effective; there is reasonable assurance of the safety and effectiveness of devices intended for human use; cosmetics are safe and properly labeled, and; 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.

Statutory Mandates

A myriad of statutory requirements translate FDA's broad mission into specific performance expectations. Two statutory categories that are central to the Agency's mission are specified time frames for review of new drug, medical device and food additive applications and frequency of inspections of drug, biologics and medical device establishments. Section 406(b) of FDAMA directed FDA to develop a plan for meeting these and other statutory requirements. The FDA Plan for Statutory Compliance was completed in November and submitted to Congress. It includes a complete listing of the Agency's statutory requirements, and is available at the following Internet address: <http://www.fda.gov/opacom/7modact.html>.

Emerging Environmental Challenges

FDA must address a wide range of challenges that serve as potential obstacles to successfully carrying out its health protection mission and meeting its key statutory mandates.

- **Greater Regulatory Volume and Complexity:** FDA-regulated products will be more technologically sophisticated than ever before, while providing unparalleled health benefits for the U.S. public. Each year, FDA-regulated firms spend an additional \$2 billion on domestic research and development. For pharmaceuticals alone, this effort currently exceeds \$20 billion--triple the amount of 10 years ago. This level of investment in new product development has a direct effect on the volume and complexity product applications requiring FDA evaluation.

- **Increase in Adverse Events:** A parallel trend to greater availability of health-enhancing products has been an increase in the number of adverse events associated with product use. Although the benefits of these products greatly outweigh the associated adverse effects, these problems must still be addressed. FDA received more than 250,000 reports of suspected drug-related adverse events in 1997, and the number continues to increase annually.
- **Emerging International Regulatory Challenges:** New products will be developed, produced and marketed in a highly networked and global commercial system. This system will have increased capability to satisfy consumer needs, but its complexity, coupled with the growing volume of international trade, will make monitoring for potential risk more difficult.
- **Persistent Threats to the Public Health:** Threats to the public health posed by products such as tobacco, and other challenges such as bioterrorism, will continue to require new regulatory responses.

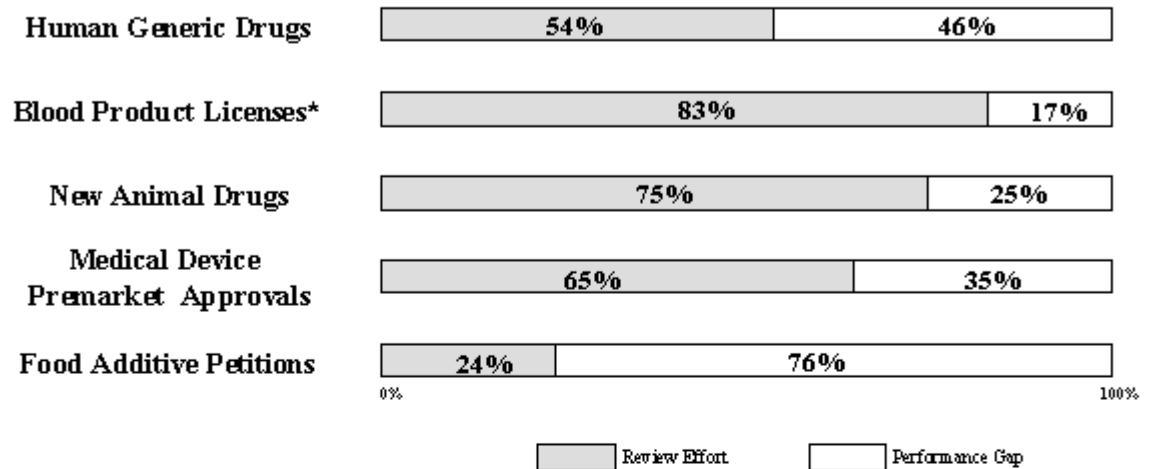
The Gap Between Expectations and Actual Performance

The environmental challenges discussed above are significant because they essentially define the nature and size of the workload that FDA will have to address in the future. To the extent that these factors can be correctly anticipated, the Agency can estimate the gap between expected and actual performance. But these estimates will change because the forces themselves are dynamic. No one knows with precision what the level of industry research and development will be even next year; medical breakthroughs cannot be scheduled, and most health or safety crises cannot be predicted. For example, it is difficult to use a durable set of cost figures to determine the level of resources that will be required to review next year's submissions of new drug applications.

However, the Agency can assert that the convergence of complex environmental challenges and sharp federal budget constraints has prevented FDA from fully meeting its explicit statutory obligations. A sizable gap still exists between statutory time requirements and actual performance for application review in several product areas (Figure 2). There is a similar gap between mandated and actual inspectional coverage for FDA-regulated industries. (Figure 3). Additional gaps exist between public expectations and current federal capability. The U.S. public expects and deserves a coordinated food safety assurance system, but one is not presently in place. In addition, the Agency has not yet initiated a comprehensive system of surveillance that can monitor, detect and correct adverse experiences associated with use of FDA-regulated products. Finally, our nation's youth continue to use tobacco without an adequate monitoring system in place to prevent illegal sales of tobacco to this segment of the population. The FY 2000 budget increases will help to narrow many of these gaps, but they will not be completely eliminated with these resources alone.

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 Interval

Biennial: Drug, Biologic, & Device Manufacturers* (16,000)

58% Inspected within 2 years

No Statutory Interval

Four-Year Average ** Cycle: Food Establishments (49,000)

59% Inspected within 4 years

Four-Year Average ** Cycle: Drug, Biologic, & Device Facilities not included in Biennial Requirement (33,000)

38% Inspected within 4 years

0%

100%

Inspection Effort

Performance Gap

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

** Selected high-risk categories inspected more frequently.

Stakeholder Consultation

FDA solicited the viewpoints of its stakeholders in a series of public meetings during the summer of 1997, and through public dockets and electronic communication. Stakeholders were asked to give their views on FDA's key priorities, and the strategies that would be most effective in closing the gap between what FDA was required and expected to do, and what it is currently able to accomplish. Since FDA's many stakeholder groups are a heterogenous population with diverse interests, their collective viewpoints did not converge on a definitive list of programmatic priorities. Two general themes, however, did emerge:

- **Encourage 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. Synergies can also be created in these collaborative arrangements which will allow FDA to narrow the performance gap in a more cost-effective manner. 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.
- **Engage in 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.

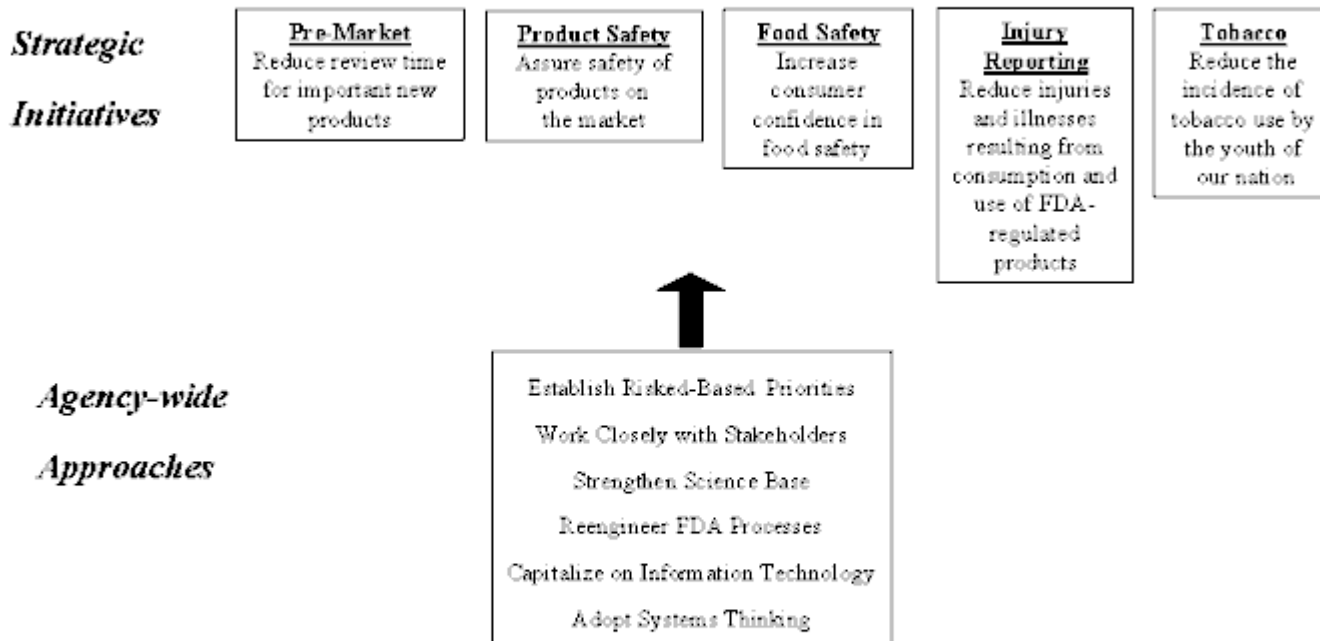
The above two themes provide the Agency with important signals on the kinds of Agency-wide approaches to which stakeholders would be receptive, and which would constitute critical elements of any specific initiative undertaken in the future. The process of engaging the Agency's stakeholders and receiving useful feedback is an ongoing one. The Agency's various constituencies will continue to play an integral role both in the formulation of specific risk management strategies, and in broad strategic assessment of FDA's overall directions.

Strategic Initiatives/Agency-wide Approaches

Through the assessment described above, FDA has formulated five strategic initiatives, each of which addresses a critical public health or safety challenge that affects major segments of the U.S. population. Successful pursuit of these initiatives will produce results that effectively close the gap between expectations and the current reality. FDA will implement these initiatives by applying approaches that collectively represent FDA's corporate philosophy. They describe how the Agency intends to operate in order to satisfy its mission and be responsive to the expressed needs of its stakeholders. Figure 4 illustrates how these approaches will be key to the Agency's successful accomplishment of each initiative.

Figure 4

FDA's Strategic Initiatives Are Supported By Agency Wide Approaches



The following two sections describe these Agency-wide approaches and give an overview of each of FDA's five strategic initiatives.

Agency-wide Approaches

Establish Risk-Based Priorities: FDA 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. Given 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. The Agency has and will continue to increase the efficiency of "fast track" processes so that the most urgently needed therapies can enter the marketplace rapidly. Surveillance and compliance efforts will also continue to be directed toward the most serious health and safety problems.

Strengthen the Scientific and Analytical Basis for Regulatory Decisions: A strong science base underpins each of the Agency's regulatory decisions, from initial research, development and testing, through production, marketing and consumption of regulated products. A strong science base consists of the necessary professional expertise, risk assessment protocols, test methods, product guidance, performance standards, and the facilities and equipment necessary for conducting excellent science. FDA continues to improve its scientific capabilities through access to and collaborative efforts with sources of scientific expertise beyond FDA.

Work More Closely With External Stakeholders: FDA will need to leverage its own capability to address complex public health problems by working with external stakeholders. Solutions to health risks do not lie solely in expanding the size 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. Cooperation with the Agency's stakeholders will be well informed by establishing and maintaining vehicles which promote continuous dialogue between FDA and its constituencies.

Re-engineer FDA Processes Where Appropriate: This principle is based on the assumption that for organizations to survive and thrive in turbulent environments, they must not be satisfied with "programmed" approaches to problem solving. FDA has redesigned many of its regulatory review processes to improve internal efficiencies. The Agency is also implementing several protocols that will result in simplified regulatory approaches, and as a result, will reduce the burden for the regulated industry.

Adopt a Systems Rather than a Piecemeal Approach to Agency Regulation: The Agency will continue to develop a systemic understanding of health and safety problems and the possible solutions to those problems. This entails an ability to explain relationships among variables in the system, to identify critical variables that drive the effectiveness of a total system, and then to direct resources more effectively to maintain those critical variables within acceptable limits. A prime example of capitalizing on systemic understanding is the implementation of the HACCP concept in food industries.

Capitalize on Information Technology: FDA has been able to take advantage of rapidly evolving information technologies to improve internal efficiencies. For example, automating major portions of the drug review process has accelerated the review of new drug therapies. 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 to consumers and patients via the Internet.

FDA Strategic Initiatives

The Agency intends to address its mission, mandates, environmental challenges and stakeholder expectations with five strategic initiatives that will be pursued in FY 2000 and beyond.

The **premarket application review** initiative addresses the proliferation of, and need for, high technology products. The Agency will continue to work closely with industry to bring new products with great health benefits to the market rapidly while ensuring their safety and efficacy.

Three initiatives--**product safety assurance, food safety, and injury reporting**--contribute to building a broad safety net that maintains high public confidence in all FDA-regulated products. FDA will collaborate with many public and private stakeholders in monitoring all phases of production and distribution, from product research and development through production, distribution and consumption. The net must have a strong science foundation and enlightened product and process standards. It must also have the ability to manage emerging risks through education, technical assistance and enforcement actions as necessary.

These three initiatives will make the following contributions:

- The Product Safety Assurance initiative aims for full inspectional coverage of domestic firms and a high level of assurance that imports entering the United States are safe.
- The Food Safety Initiative is a comprehensive, multi-agency effort designed to assure safety of the U.S. food supply.
- The Injury Reporting initiative proposes a coordinated system of problem reporting and correction resulting from adverse experiences with FDA-regulated products.

The fifth initiative, regulating **Tobacco**, targets a pervasive, high-risk area that threatens the health of a large portion of the U.S. population. FDA has identified the reduction of tobacco use by the youth of this nation as a major strategic focus. The Agency will work closely with states and other stakeholders to reduce young people's access to tobacco and lessen the appeal of tobacco products.

A full explanation of the five initiatives follows, including a description of the challenge posed by the environment and FDA's plan to meet the challenge and measure its success.

Premarket Application Review

Intended Outcome: Reduce the time required to make important new human drugs, veterinary drugs, blood products, medical devices, vaccines and food additives available to the U.S. public.

Background: The nation's (and world's) research and development community continues to proliferate many new, and often technologically complex, products with health-giving properties. FDA will continue to facilitate their availability. FDA is also required by the Food, Drug and Cosmetic Act to review new product applications within specific time

frames. The need to meet these time frames has been reinforced by the recent FDA Modernization Act of 1997.

FDA continues to make significant strides in accelerating approvals of new drugs and biological products. In 1998 the Agency approved 90 original new drugs, with a median approval time of 12 months. Of these approvals, 25 were for priority products considered to be of exceptional public health value. The priority products were approved in a median time of 6.4 months.

The Agency has made these product review improvements under commitments made in association with the Prescription Drug User Fee Act. However, the Agency has not been able to meet statutory time frames in other key product areas.

FDA's Plan: FDA will focus its efforts on accelerating reviews in the product areas that are not currently meeting the premarket review time frames defined by law and by the expectations of FDA's stakeholders. These areas include: medical devices, blood products, generic human drugs, veterinary drugs and food and color additives. Several interlocking strategies will be used to meet these review goals. First, the Agency will dedicate additional reviewers to these high-priority areas. To ensure wise use of reviewers' time, the FDA has re-engineered 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 likelihood 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.

How performance will be measured: For programs in which information systems are mature, performance will be measured by faster review times. For programs which are being re-engineered and/or new regulatory approaches are being used, performance will be gauged by milestones which mark the implementation of new information systems, regulatory approaches, and management mechanisms.

Product Safety Assurance

Intended Outcome: Assure that FDA-regulated products are being produced and marketed under conditions that will assure their safety, quality and efficacy.

Background: FDA's ability to guarantee the quality and safety of all regulated products from domestic and foreign sources is declining. The Agency, even with the help of its state partners, and with projected resource increases in FY 2000, is falling considerably

short of conducting the biennial inspections of drug and medical device firms required by law. The average food plant is inspected less than twice a decade, a frequency far below public expectations. Although the Agency reviews nearly four million import shipments of regulated products each year, it directly examines only a very small percentage of these entries. In addition, import entries continue to grow in number, complexity, and in diversity of sources. To illustrate, in 1997 over \$10 billion in pharmaceuticals and medical devices were imported into the United States from the European Union (EU). By the year 2000, FDA may be equipped to handle less than one inspection per \$100 million in EU pharmaceutical exports. The Agency needs a way to verify the safety of imports from point of origin through point of entry.

FDA's Plan: FDA intends to meet its domestic statutory requirement by inspecting domestic firms more often with the assistance of our state regulatory counterparts. The Agency will also use multiple strategies of education, technical assistance, targeting higher risk industry sectors, and enforcement (when necessary) to correct product risk in the market place. A key element of assuring quality and safety, particularly in the food industry, will be to strengthen the ability of industry to develop its own safety and quality monitoring systems. This will be accomplished by expanding the Hazard Analysis and Critical Control Point (HACCP) program from seafood to other industry segments. To improve monitoring of imports, FDA will continue to cooperate with the U.S. Customs Service and build on the early successes of our electronic import entry system. Currently, more than half of FDA's import categories are electronically screened based on historical data, and allowed entry to the U.S. within 15 minutes. The enhanced entry system will also provide the Agency with national "electronic profiles" of high-risk imports, which can then be more effectively targeted through a selected sampling program. While improving import safety at the border, FDA will also be strengthening surveillance at the source of production. Finally, the Agency will continue to work on international preventive strategies through participation in international standard setting and mutual recognition of safety assurance.

How performance will be measured: For domestic industries, performance will be measured by the increasing portion of the industry that will be covered by inspections, and by the rate of conformance to FDA regulations. Industry's ability to self-monitor will be measured by the percentage of firms in a target sector that have successfully installed these systems. For the import sector, effectiveness in allowing safe products to enter the country will be measured primarily by the percentage of products for which FDA can make rapid and reliable entry decisions.

Food Safety

Intended Outcome: Increase consumer confidence in the safety of the nation's food supply.

Background: In 1997 the United States Department of Agriculture (USDA) recalled 25 million pounds of raw hamburger because of possible *E. coli* bacterial contamination, which can cause serious illness, and even deaths. And when health officials linked a 1998 hepatitis outbreak in Michigan to frozen strawberries from Mexico, more questions arose about the source of foods on American tables. Some 40 percent of fruits and vegetables in the United States are grown outside our borders. Although overall mortality and morbidity rates resulting from foodborne contaminants are not known with precision, even the anecdotal evidence of food-related illness is sufficient to be disquieting.

At the President's urging, several federal and state agencies are collaborating in a multi-sector initiative to strengthen the nation's food safety status. This initiative combines surveillance, compliance, research, risk assessment and education. Thus, the Food Safety Initiative contains all of the elements necessary to weave an impressive safety net in which FDA plays a central role. The Agency is home to expert food scientists, and a substantial portion of the field force is dedicated to the assurance of food safety in domestic firms. However, for a truly collaborative inter-agency, inter-sector system to work effectively, time will be required to coordinate various research protocols, standards, information systems and other institutional arrangements.

FDA's Plan: There are two key elements in FDA's Food Safety Initiative. First, the Agency will expand its research, risk assessment, surveillance, compliance, and educational capabilities and focus this expertise on the highest priority food safety risks. Second, FDA will strengthen its capability to work collaboratively with Department of Agriculture (USDA), the Centers for Disease Control and Prevention (CDC), the Environmental Protection Agency (EPA), the states, and the regulated industry. This will require the development of risk assessment priorities, risk management strategies, and information systems that are compatible with those of the Agency's partners. This coordination is essential so that food safety problems can be addressed quickly and effectively.

How Performance Will Be Measured: Progress in the Food Safety Initiative will be measured primarily by milestones which demonstrate that critical components of the food safety net are being put into place. One of those critical elements is a food safety surveillance system that will track the health and safety outcomes of this initiative.

Injury Reporting

Intended Outcome: Reduce injuries and illnesses resulting from consumption and use of FDA-regulated products.

Background: A 1998 study published in the Journal of the American Medical Association (JAMA) estimates that nearly 7 percent of hospitalized patients suffer a serious or fatal reaction to drugs administered during their hospital stay. This would make

such adverse reactions to prescription drugs the fourth leading cause of death in America, behind heart disease, cancer, and stroke.

There is no comprehensive surveillance system in place to accurately identify the number of adverse events that are associated with use or consumption of FDA-regulated products, to evaluate the cause of these incidents, or to formulate the strategies needed to avoid similar future incidents. Existing passive reporting systems are not adequate to gauge the scope of these problems. Consequently, neither FDA nor its health and regulatory partners have precise data on the magnitude of the adverse event problem. However, several reporting systems exist, both within FDA and in other organizations. The challenge is to determine which elements of existing systems can be capitalized upon, and what new aspects will be needed for a comprehensive system.

FDA's Plan: FDA is currently determining which elements of a comprehensive reporting and intervention system can be centralized and which should remain tailored to the needs of our respective product centers. In the process of reaching out to its partners in this area, the Agency will capitalize on existing collection and reporting systems. FDA will also build a surveillance system that will use representative samples to collect information based on epidemiological data and known relative risks. The overall strategy combines elements of surveillance, problem analysis, education and problem correction through elimination of the conditions that led to the high-risk situation.

How Performance Will Be Measured: Performance will be monitored by the milestones that mark implementation of a comprehensive adverse event reporting and intervention system. As in the case of food safety, once the key elements of this system are in place, it should provide the Agency with a future capability to track health and safety outcomes that result from Agency strategies.

Tobacco

Intended Outcome: Reduce the incidence of tobacco use by the youth of our nation.

Background: Every day about 3,000 young people begin smoking, and it is estimated that 1,000 of them will die prematurely. In fact, 34 percent of high school students know the dangers and still smoke. Americans pay \$50 billion annually in medical costs to treat the cancers, lung disease, strokes and other ailments attributed to this addictive and deadly behavior. FDA has the support of the American people to regulate the use of cigarettes and smokeless tobacco. Tobacco is a major Presidential Initiative, and is receiving the support and cooperation of several federal and state agencies, including FDA. FDA has already issued regulations that prohibit retailers from selling tobacco to underage smokers, and require them to check photo ID's of all customers 27 years of age or younger. Resources have been proposed that will allow the Agency to initiate other aspects of this program.

FDA's Plan: The major components of the FDA strategy include: restricting access to tobacco; educating retailers about the new regulations; and beginning to implement processes for regulating tobacco. While the third strategic component is still pending, FDA is embarking on retailer compliance checks and retailer education. FDA's strategies are complementary to those of other federal agencies such as the CDC, the Substance Abuse and Mental Health Services Administration (SAMHSA), and the National Cancer Institute (NCI). These partners are focusing research on the effects of smoking, long term education of the population, monitoring outcome data on smoking cessation, and on determining morbidity and mortality rates.

How Performance Will Be Measured: During FY 1999 and 2000, FDA's progress in the tobacco initiative will be measured by: 1) the degree of coverage achieved in conducting compliance checks among the estimated 500,000-1,000,000 tobacco retailers, and 2) the awareness levels of retailers concerning existing regulations. Outcomes such as smoking rates and mortality and morbidity figures will be monitored by FDA's sister agencies. The results of outcome monitoring will serve as input to adjusting any tobacco program strategies.

Coordination Across Organizations

Each of these strategic initiatives supports the FDA mission, as well as the objectives outlined in the strategic plan of the Department of Health and Human Services (DHHS), FDA's parent department (see Table A).

Table A
FDA Strategic Initiatives Relate to DHHS Strategic Objectives

DHHS Objectives	FDA Strategic Initiatives				
	Premarket Application Review	Product Safety Assurance	Food Safety Initiative	Injury Reporting	Tobacco
Reduce the major threats to the health and productivity of all Americans.		✓	✓	✓	✓
Improve the economic and social well-being of individuals, families, and communities in the U.S.	✓	✓	✓	✓	✓
Improve the quality of health care and human services.	✓	✓		✓	
Improve public health systems.	✓	✓	✓	✓	✓
Strengthen the nation's	✓	✓	✓	✓	

health sciences research enterprise and enhance its productivity					
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Table B illustrates how the responsibility for achieving the five major multi-year initiatives previously outlined is shared across FDA program areas.

Table B
FDA Strategic Initiatives Relate to Agency Programs

FDA Programs	FDA Strategic Initiatives				
	Premarket Application Review	Product Safety Assurance	Food Safety Initiative	Injury Reporting	Tobacco
Foods Program	✓	✓	✓	✓	
Human Drugs Program	✓	✓		✓	
Biologics Program	✓	✓		✓	
Medical Devices and Radiological Health Program	✓	✓		✓	
Animal Drugs and Feeds Program	✓	✓	✓	✓	
National Center for Toxicological Research	✓	✓	✓	✓	
Tobacco Program					✓

FDA's Role as an NPR High Impact Agency

FDA is one of thirty-two federal agencies that have been designated "High Impact Agencies" by the National Partnership for Reinventing Government, primarily because they have the most interaction with the public and business. These agencies will work with NPR over the next three years to transform themselves into customer-oriented, results-driven organizations. The leaders of these agencies have each committed to a small number of significant, measurable goals that can be achieved over the next three years.

FDA's proposed reinvention goals are critical for the Agency's successful performance in the 21st century. Each of the goals requires new ideas, responsiveness to our "customers" (the American public) and close cooperation with key stakeholders. FDA will achieve the goals listed below provided that the current and projected funding levels for these initiatives are maintained.

More Efficient Drug Development: By the year 2000, reinvent the drug development and review process, thereby lowering the development costs, and, more importantly, reducing by an average of one year the time required to bring important new drugs to the

American public. FDA will accomplish this through early and frequent consultation with product sponsors, implementation of an automated application filing process, and reauthorization of an enhanced user fee program.

- Supported by the Human Drugs goals on pages 58 and 59

Better Medical Product Information: In accordance with legislative mandate, 75 percent of all consumers receiving new drug prescriptions will be given more useful and readable information about their product by the year 2000. Usefulness is defined in terms of: scientific accuracy; unbiased content and tone; specificity and comprehensiveness; and timeliness. Based on national surveys conducted by FDA, the percentage of people who received useful information on new drug prescriptions was only 32 percent in 1992. To achieve the 75 percent goal, FDA will work closely with industry, health care providers and the consumer. Simultaneously, FDA will revise prescription drug and OTC labels to make them more readable. These information and labeling initiatives will improve the accurate use of medications and reduce risks associated with medication misadventures.

- Supported by the Human Drugs goals on pages 61 and 62

Stronger Food Quality Assurance: By the end of FY 2000, assure improved quality of the American food supply, through a collaborative system encompassing government and private sector stakeholders.* Eighty percent of the domestic seafood industry will be operating preventive controls as evidenced by functioning HACCP (Hazard Analysis Critical Control Point) quality control systems. HACCP is a newly instituted, industry-based monitoring system, and represents one element in the President's multi-strategy Food Safety Initiative. FDA will be working closely with USDA, EPA and the Centers for Disease Control and Prevention to implement this initiative.

* Assumes funding of the Food Safety Initiative through the year 2000.

- Supported by the Foods goal on page 39

Faster Access to Important New Medical Devices: By the year 2000, reduce the review time for important medical devices by 60 percent. (Important medical devices are products that present a major clinical benefit or those that may pose a significant risk to patients). This will be accomplished by reinventing the screening and review process for product applications. The impact of this goal is that millions of Americans will have faster access to safe and effective medical devices. FDA is reinventing the medical device review process and redefining the concepts of high risk and high impact products. The new definition will be applied to establish a baseline to measure review time for important medical devices.

- Supported by the Medical Devices and Radiological Health goals on pages 98 and 99

The priorities represented by these four goal statements overlap with those described in FDA's Agency Performance Plan. Performance goals that support the accomplishment of these High Impact Agency goals are noted as such in Part Two of this plan.

Part Two: FDA's FY 2000 Performance Goals

As You Read FDA's Performance Plan Part Two...

As you read the performance goal section of the Performance Plan, you may wish to note these important points.

FDA's 2000 Plan:

Σbuilds on the 1999 Performance Plan. FDA's Year 2000 Performance Plan refers frequently to FY 1999 performance goals. While some goals have been changed or added, others may have been deleted in favor of goals that are more critical to current health concerns. A summary of the status of FDA's FY 1999 goals, with explanations of revisions to the goals, appears in Appendix 1. Appendix 2 provides a complete listing of FY 1999 and FY 2000 goal commitments.

Σresponds to guidance from Congress. The 1993 Government Performance and Results Act (GPRA), along with the Department (DHHS), place great value on achieving meaningful results through strategic planning. In the Year 2000 Performance Plan, FDA emphasizes the anticipated long-term results that can be achieved by reaching the performance goals set for the year 2000.

Σexplains the rationale for each strategic goal. Each of FDA's seven major program areas has included important information explaining why their major goals are important to protecting public health. By providing this context, readers should understand the rationale for each goal, as well as gain an appreciation for the investment needed.

Σtracks important data needed to measure progress. Whenever data are available, FDA includes that information to help track progress toward achieving each goal. In some cases, the data are already valid and reliable indicators of progress. In other cases, new ways of gathering meaningful data may be needed to monitor progress toward a goal. Data issues are addressed for each goal.

Σoutlines the resources needed to achieve results. The proposed investment in dollars and personnel is shown for each FDA program area.

Σhighlights our many partnerships. Because our mission is complex and affects so many products and all Americans, we work closely with scientists, health officials, policy makers, educators and the public. Some of our most important partnerships are highlighted in the plan.

Part Two describes the specific performance goals necessary to implement the strategic initiatives. The performance goals are organized by the Agency's program areas which also serve as the major categories in the Agency's budget. It is the responsibility of the managers within these programs to carry out the strategies necessary to achieve the performance goals.

The seven program areas within FDA's budget, and their functions, are:

- **Foods:** Ensures that the nation's food supply is safe, nutritious, wholesome, and honestly labeled. It also ensures that cosmetics are safe and properly labeled.
- **Human Drugs:** Ensures that all drug products used for preventing, diagnosing, and treating disease are safe and effective; and that information on their proper use is available.
- **Biologics:** Ensures the safety, potency, and effectiveness of biological products for the prevention, diagnosis, and treatment of disease. Included are blood and blood products, test kits, vaccines and antigens, therapeutic agents, and other biologicals.
- **Medical Devices and Radiological Health:** Ensures that medical devices are safe, effective, and properly labeled; and that the public is not exposed to excessive radiation from medical, industrial, and consumer products.
- **Animal Drugs and Feeds:** Ensures that only safe and effective animal drugs, devices, feeds, and food additives are marketed; and that foods and food additives from animals that are administered drugs are safe for our consumption.
- **National Center for Toxicological Research:** Implements peer reviewed, high-quality scientific research to develop methods for regulatory applications and provide a mechanistic basis for human risk assessment as it pertains to FDA's regulatory mandate.
- **Tobacco:** Works to reduce young people's use of tobacco through education, enforcement, and partnerships with other federal and state health agencies.

Within each program area, there is a **Verification and Validation** section which addresses types of data sources used for measurement, reliance on current data sources and plans for enhancements, and limitations of the data.

Appendices

Appendix 1: Documents the current status of FDA's previously published FY 1999 performance goals.

Appendix 2: Provides a summary of FDA's FY 1999 and FY 2000 performance commitments.

Appendix 3: Focuses on FDA's import strategy. In this section, the Agency outlines its plan for ensuring the safety of all imports entering the United States. All of FDA's program areas contribute to the import initiative and the import effort is reflected in each of the program sections as well as in this appendix.

Appendix 4: A glossary of acronyms used in this document.

FY 2000 Program Resource Summary by Strategic Goal Area

Program/Strategic Goal Area	Dollars (\$000)	FTEs
FOODS	275,955	2,478
Availability of Safe, Healthful Food Products	31,294	244
Foodborne Illness Prevention and Control	223,835	2,047
Intelligence on Food-related Injuries and Outbreaks	11,026	90
Nutrition Content, Cosmetics and Fraud	9,800	97
HUMAN DRUGS	316,760	2,565
Access to Safe, Effective Drugs	198,780	1,855
Injury From Adverse Reactions or Medication Errors	46,592	126
High-Quality Drugs	71,388	584
BIOLOGICS	138,114	1,067
Availability of Safe, Effective Drugs and Biologics	30,685	187
Safety of Blood and Blood Products	72,286	542
Compliance in Manufacture of Biologics	35,143	338
ANIMAL DRUGS AND FEEDS	52,473	469
Availability and Diversity of Safe Animal Products	17,515	207
Unsafe or Illegal Use of Products	27,258	232
Foodborne Illness	7,700	30
MEDICAL DEVICES AND RADIOLOGICAL HEALTH	186,051	1,633
Safe, Effective Devices Reviewed On Time	70,325	639
Safe, Effective Mammography Facilities	21,317	147
Detection and Prevention of Problems and Injuries	19,199	151
Domestic and Foreign Inspection Coverage	49,862	448
Science-Based Quality Assurance	14,374	137
Beneficial Use of Radiation at Minimal Risk	10,974	111

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH	33,679	227
New Strategies For Prediction of Toxicity	16,645	114
Computer-based Predictive Systems	4,714	32
Method, Agent and Concept-Driven Research	12,320	81
TOBACCO	68,000	40
Reduce Access to and Appeal of Tobacco to Children	42,000	29
Enlist Retailers to Reduce Children's Use	22,000	6
Establish Regulatory Procedures for Tobacco Products	4,000	5

Resource amounts are based on FY 2000 Request and include Budget Authority and User Fees.

FOODS

Total Program Resources (FY 2000):	\$000	FTEs
Center	126,011	895
Field	149,944	1,583
Total	275,955	2,478

Program Overview

A safe, nutritious and wholesome food supply is important to the health and well being of each citizen and the nation as a whole. Although the U.S. food supply is reputed to be one of the safest in the world, much can be done to improve the protection provided to consumers. This fact is clearly illustrated by the high yearly cost in human illness, medical expense, and lost wages caused by food-related infections. The United States Department of Agriculture's (USDA) Economic Research Service (ERS) has estimated that every year up to 81 million illnesses and as many as 9,000 deaths can be attributed to foods. ERS also estimated that the cost of medical treatment and lost wages associated with these illnesses ranges between \$6.6 and \$37.1 billion.

In its recent report on imported foods, the Government Accounting Office (GAO) indicated that "ensuring the safety of domestically produced foods is a daunting task, but the challenge of ensuring the safety of the entire food supply is even more difficult as Americans consume more imported foods." This is part of the reality FDA faces in its mission to develop and maintain the regulatory, research, and other capabilities required

to protect consumers from harmful domestically produced or imported food products. FDA is responding to a rapidly growing number of complex and challenging food safety issues. These include emerging pathogens, natural toxic constituents in foods, macro food ingredients, hazardous dietary supplements, pesticides and industrial chemical contaminants, biotechnology products, new processing systems, and the rapidly increasing numbers of foods imported from foreign nations. Strategies to address these important food safety issues must be innovative, based on sound science, and effectively coordinated with the Agency's federal partners and the states.

Since FY 1996, FDA has worked more cooperatively with its federal partners to enhance the safety of the nation's food supply. The goals and objectives of these government-wide efforts were established through two Presidential Initiatives on food safety. The first focused on enhancing surveillance of foodborne disease outbreaks, improving inspection and compliance, targeting important new research and risk assessment initiatives to fill critical gaps in food science, and expanding food safety education and training, especially for those who handle food at critical points from the retail setting to the home. A second Presidential Directive, issued on October 2, 1997, focused on actions to improve the safety of domestic and imported fresh fruits and vegetables. These initiatives respond to the increasing number of foodborne illness outbreaks, especially those caused by the sudden appearance of newly recognized pathogens, and the public's increasing concern for the safety of foods available in the marketplace.

Although the first phases of the Food Safety Initiative (FSI), funded in FY 1998, provide much-needed resources to deal with critical food safety issues, namely those related to bacterial contamination and mycotoxins, a number of other foodborne contaminants threaten the health and well being of consumers. These include a wide range of pesticides and industrial chemical contaminants and natural toxins. The safety of dietary supplements and other nutrition supplements is another concern. Also, while food labeling is most critical for those who are subject to allergic reactions to food ingredients, it provides information that helps consumers make more healthful dietary choices and avoid the effects of diet-related diseases such as heart disease, stroke, and certain cancers.

Over the past several years, another major focus of the Food Safety Program has been streamlining the process for premarket reviews of food and color additive petitions. Significant steps have been taken to make this process more efficient and reduce the number of overdue food and color additive petitions. These steps include management improvements, modernization of the electronic information infrastructure to increase efficiency, reallocation of resources from other program activities to petition review, and extramural contracts to provide for third-party reviews of scientific data supporting petitions. In FY 2000, the Agency is requesting authorization to establish user fee programs for food additive petition reviews and reviews of premarket notifications for food contact substances (indirect food additives). If Congress grants this authorization, the Agency will have a stable source of resources to increase significantly the speed of petition and premarket notification reviews and improve its ability to meet statutory time frames for completing these reviews.

In this plan, FDA's food safety activities are organized into four strategic goal areas: Product Safety Assurance; Injury Reporting; Premarket Application Reviews; and Food Labeling, Cosmetics and Economics. Product Safety Assurance, the largest goal area, includes compliance monitoring, program coordination, food safety education, and the bulk of the Program's food safety research and risk assessment activities. Activities in the Injury Reporting strategic goal include injury surveillance, adverse event reporting, epidemiology, consumer studies and other activities that provide information on the numbers, trends and types of foodborne illnesses. The Premarket Application Review goal includes activities to ensure that food and color additives are safe, infant formulas are safe, and health claims are scientifically valid. Activities in the Food Labeling, Cosmetics and Economics strategic goal include nutrition policy and other activities related to food labeling, cosmetics safety, and activities related to protecting consumers from economic fraud. The activities in each goal area make important contributions to efforts to protect the public health.

Program Strategic Goals

Strategic Goal 1:

Reduce the possibility of food-related injuries and improve the health and well being of consumers by ensuring that decisions related to approving petitions and notifications are scientifically justified and benefit the public health.

Resources: \$31,294,000 244 FTEs

Performance Goals:

- Complete first action (i.e., review all parts of the petition and issue a "not approvable" letter, or publish a response in the *Federal Register*, if appropriate) on 40 percent of food and color additive petitions within 360 days of receipt. ⁽¹⁾
- Reduce the percentage of overdue food and color additive petitions (i.e., under review for more than 360 days) to 20 percent of petitions under review.
- Complete initial processing of 80 percent of biotechnology consultations within established time frames.
- Complete processing of 80 percent of Generally Recognized as Safe (GRAS) notifications within the time frame established by the final rule.
- Finalize guidance and regulations necessary to support operations of the premarket notification program for food contact substances established by the FDA Modernization Act and as set out in Sec. 409(h) of the Federal Food, Drug, and Cosmetic Act.
- Respond to 95 percent of nutrient content claim and health claim petitions/notifications within the statutory and regulatory time frames.

Rationale:

Under several statutes, including the Federal Food, Drug, and Cosmetic Act (FD&C Act) and Nutrition Labeling and Education Act (NLEA), FDA has authority to ensure that food ingredients and infant formulas are safe and that health claims are based on sound science. The Agency also has premarket notification programs for GRAS substances and biotechnology products and is required under the Food and Drug Administration Modernization Act (FDAMA) to establish similar procedures for food contact substances.

Under the FD&C Act, food and color additives are required to undergo premarket review before entering commerce. To initiate this premarket review, sponsors are required to submit a petition including appropriate test data to demonstrate the safety of the intended use of the substance. Once the review is complete, the Agency is required in many cases to publish its decision in the *Federal Register*. Under the premarket notification program for food contact substances established by FDAMA, industry will submit a notification to FDA 120 days prior to marketing a food contact substance. If FDA does not object during the 120-day review period, the notifier may legally market the substance for the use described in the notification.

This strategic goal includes all premarket review and consultation activities within the Foods program that are associated with food additives, color additives, GRAS food ingredients, and foods derived from new varieties of crop plants using biotechnology. These premarket activities must implicitly or explicitly address the question of whether a substance or product is safe for human use.

Under NLEA, FDA must ensure that nutrient content claims and health claims that appear on food product labels comply with its regulations or are based upon an authoritative statement of a scientific body of the U.S. Government. NLEA and FDA regulations specify the time frames within which FDA must act on submissions for approval of these claims. FDA's timely response to these submissions enables industry to plan more efficiently its introduction of products to the marketplace.

The Infant Formula Act of 1980 and later amendments protect infants and young children by requiring that infant formula companies notify the FDA before offering a new formula for sale, when changing processing methods or formulations, and when the company has reason to believe a formula does not meet the requirements of the Act or is otherwise adulterated or misbranded. Infant formula submissions are to be reviewed and a response issued to the company within the prescribed time limit of 90 days in those cases where FDA determines that there is a potential problem.

Since the objective of premarket reviews is to prevent exposure to hazardous substances and to prohibit scientifically unsupported health claims, their contribution to disease prevention and health is undeniable. However, performance outcomes cannot be clearly identified or measured without data systems that can directly link these activities to incidence of disease. The Agency is exploring ways to assemble the types and amounts of data required to establish realistic performance baselines for its food-related premarket review activities.

Approaches, Skills, Technology, and External Factors:

Food and Color Additives

In keeping with FDAMA and stakeholder requests for an FDA that is more open and transparent about its processes and procedures, a major objective for FY 2000 will be to improve the quality of incoming petitions. This will be accomplished with the appropriated increase by offering more assistance to potential petitioners during the petition development process and during the post-filing review process. To achieve this, FDA plans to develop and publish comprehensive guidelines for petition preparation, and to design and develop an education program explaining the types of studies and safety data required to support petitions. The Agency also plans to consult extensively with potential petitioners before they file, and will work closely with petitioners after they have filed to resolve quickly any problems encountered during review. Multidisciplinary review teams will be created to help rapidly resolve new and ongoing safety issues related to petition reviews. Moreover, additional resources will be devoted to administrative record keeping to enhance internal processing of petition review information.

In mid-FY 1997, FDA changed its procedures, and first actions were redefined as a review of all parts of a petition, followed by issuance of a "not approvable" letter, or publication of a response in the *Federal Register*, if appropriate. Previously, as a petition was reviewed, whenever a deficiency in any one area was found, the petitioner was notified and asked for the information, and review of the remainder of the petition was suspended. This notification was counted as a "first action." The effect of this policy was to increase the percentage of first actions completed in a given time frame, compared to what would have been the case if FDA initially examined the entire petition.

If Congress authorizes user fees for food additives, FDA will establish user fee programs for direct food additive petitions and indirect food additive (food contact substances) notifications. These user fee programs, which are supported by industry, would provide a stable source of resources that will permit the Agency to significantly enhance the efficiency of the review processes for food additives. Fees assessed for the review of direct food additive petitions would provide the resources needed to substantially increase the speed of the review process, permit the Agency to meet established time frames for these reviews more consistently, and provide the type and level of assistance required to help petitioners significantly improve the quality of their submissions. User fees would also permit FDA to establish the premarket notification (PMN) procedure for food contact substances as outlined in FDAMA. The notification procedure for food contact substances has not been implemented due to a provision in the FDAMA legislation that stipulates that the program can only commence when certain funding requirements are met. Although FDA received an increase in appropriated funds in FY 1999 for this effort, the resources appropriated are not adequate to establish the systems and regulations that are necessary to implement the program.

Health Claims and Infant Formula Notifications

FDA maintains a cadre of scientists and other specialists to review and act on nutrient content claim and health claim petitions and notifications without delay. FDA also consults with other agencies in DHHS and USDA on the appropriateness of claims and their justification.

The review of Infant Formula Notifications requires a staff of highly trained people, including Medical Officers, Consumer Safety Officers and Nutritionists with knowledge of the nutrient requirements of infants. Review material consists of company formulations, rationale for formula change, clinical studies of the new or changed formula, and other relevant material. FDA must review these submissions within the 90-day time limit and report results of the review to the company. In addition, FDA must review other changes or issues that arise during the year and provide comments to the company within narrow time limits.

Assumptions: The FY 2000 performance goals of this strategic goal area assume that FDA will receive the resources requested in the budget to enhance the premarket application review process and that the petition/notification workload will not increase significantly. If the statute is amended to authorize the collection of user fees to support food and color additive petition reviews, performance goals will be negotiated with the affected industry and will be commensurate with the additional resources made available through the collection of these fees. This would have a direct impact on the performance goals established in this Plan for food additive petition reviews and could also indirectly impact the goals established for premarket notifications.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Complete first action (i.e., review all parts of the petition and issue a "not approvable" letter, or publish a response in the *Federal Register*, if appropriate) on 40 percent of food and color additive petitions within 360 days of receipt. ⁽¹⁾

Data Sources: CFSAN's electronic workflow system

Baseline Data:

FDA does not yet have quantitative baseline data comparable to this goal (see *Note about Baseline Data*). Baseline data based on the new definition of first actions will be available for FY 1999 by October 2000.

FY 1997:

For petitions received in FY 1996, using the previous petition review procedure, 24% of petitions received "first action" within 180 days.

FY 1998:

Developed and tested an electronic workflow system that will facilitate tracking and

assignment of petition reviews. Additional work required to make the system fully operational by the end of FY 1999 was not funded in FY 1998.

FY 1999:

Complete "first action" on 30% of food and color additive petitions within 360 days of receipt. The workflow system will be operational (target).

Milestones:

FY 2002:

Complete "first action" on 70% of the food and color additive petitions within 360 days of receipt (target).

FY 2004:

Complete "first action" on 80% of the food and color additive petitions within 360 days of receipt (target).

Note about Baseline Data: In this goal, "time to first action" is not the same as meeting the statutory time frame (i.e., 90 days, extendable to 180 days). It is widely recognized that meeting the current statutory time frame is an unrealistic goal for all food and color additive petitions, especially the more complex ones. Indeed, the impracticability of current time frame was acknowledged in the report from the June 1995 hearing before Congress, and a recommendation to change the time frame was included in the Agency's testimony before the House Committee on Government Reform and Oversight in 1996.

Goal Statement: Reduce the percentage of overdue food and color additive petitions (i.e., under review for more than 360 days) to 20 percent of petitions under review.

Data Sources: CFSAN's electronic workflow system

Baseline Data:

FY 1997:

As of the end of FY 1997, 44% of petitions under active review were "overdue" (defined as under review for more than 180 days).

FY 1998:

38%. Develop electronic workflow system to facilitate tracking and assignment of petition reviews (target).

FY 1999:

30% (target).

Goal Statement: Complete initial processing of 80 percent of biotechnology consultations within established time frames.

Data Sources: CFSAN's Correspondence Tracking System and other internal CFSAN Office of Premarket Approval (OPA) databases; CFSAN's electronic workflow system

Baseline Data:

Under development. Baseline data are expected for FY 1999. The projected goal is based on the Agency's analysis of its limited tracking data and to a larger degree on FDA experience thus far with these submissions. Finally, based on the Agency's inability to control the number of submissions, we believe that the goal in this area represents full performance.

Goal Statement: Complete processing of 80 percent of Generally Recognized as Safe (GRAS) notifications within the time frame established by the final rule.

Data Sources: Internal OPA database; CFSAN's electronic workflow system

Baseline Data:

Under development. FDA currently does not have quantitative data to establish a baseline for this goal (see *Note about Baseline Data.*) Baseline data are expected for FY 1999. The projected goal is based on the FDA's analysis of its experience thus far implementing this process on an interim basis.

Note about Baseline Data: GRAS notification is a new program, and the final rule establishing the GRAS notification process has not yet been published. Thus, the final time frame upon which this goal will be measured has not been established. Nevertheless, the Agency believes, based on limited experience in the review of interim notice submissions that the above performance goal can be reached. We also believe that this represents a full performance level for this program.

Goal Statement: Finalize guidance and regulations necessary to support operations of the premarket notification program for food contact substances established by the FDA Modernization Act and as set out in Sec. 409(h) of the Federal Food, Drug, and Cosmetic Act.

Data Source: *Federal Register*

Baseline Data:

Systems to collect data to establish baselines are under development and will be implemented when the program for food contact substances is developed and becomes operational.

Goal Statement: Respond to 95 percent of nutrient content claim and health claim petitions/notifications within the statutory and regulatory time frames.

Data Sources: Internal data systems.

Baseline Data:

FY 1996:

All four health claims received were processed in statutory time frames.

FY 1997:

Received and processed one health claim.

FY 1998:

Received and processed three health claims.

FY 1999:

Receive and process three health claims (target).

Strategic Goal 2:

Reduce foodborne illnesses by expanding the use of preventive control systems, expanding compliance monitoring of domestic and imported products, increasing the public's understanding and use of safe food handling practices, and developing more effective techniques for detecting, preventing and controlling foodborne hazards.

Resources: \$223,835,000 2,047 FTEs

Performance Goals:

- Eighty percent of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning Hazard Analysis Critical Control Point (HACCP) systems.
This goal supports the accomplishment of the NPR High Impact Agency goal, Stronger Food Quality Assurance
- Increase the frequency of high-risk domestic food establishment inspections to once every one to two years, and annually beginning in FY 2001.
- Assure that FDA inspections of domestic food establishments, ⁽²⁾ in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.
- Initiate Hazard Analysis Critical Control Point (HACCP) systems in the juice industry.
- Continue to develop and implement voluntary guidance and other efforts to improve the safety of fresh fruits and vegetables, and work with USDA to conduct a 1999-2001 National Agricultural Statistics Survey (NASS) of microbial contamination of fresh produce to collect the data required to evaluate program effectiveness.
- Increase the number of inspections/evaluations of foreign food establishments from 100 to 250.
- Achieve adoption of the Food Code by at least 35 percent of the states.
- Develop modeling techniques to assess human exposure and dose response to certain foodborne pathogens.

- Develop and make available an improved method for the detection of hepatitis A virus, *Cyclospora cayetanensis* and *Escherichia coli* O157:H7 on additional fruits and vegetables, and provide knowledge and technologies needed to develop guidance and methods for the control and elimination of pathogens on particular fruits and vegetables such as *Escherichia coli* O157:H7 and *Salmonella spp.* from juices, leafy vegetables and sprouted seeds, and *Cyclospora* from soft fruit (e.g., berries).
- Develop more rapid and accurate analytical methods for foodborne chemical contaminants (including bacterial toxins).

Rationale:

FDA regulates approximately 70 percent of the food supply. The products regulated are susceptible to a wide range of serious potential health hazards, including microbial pathogens, natural toxic substances, man-made chemical contaminants, and toxic elements. Hazardous nutrition supplements are also a concern. Activities in this goal area are meant to minimize the possibility that foods in the marketplace contain these or other human health hazards.

FDA's Food Safety Program must address issues that are more numerous and more complex than those faced in the past. Moreover, the scope of its regulatory responsibilities, which is already enormous, is continually growing. The Agency is responsible for regulating over 50,000 establishments that process, distribute or store food products. While the number of establishments remains relatively constant from year to year, the volume of food produced is increasing as industry produces products to meet the needs of a growing population. FDA is also responsible for ensuring the safety of a growing volume of imported foods. The number of food lots entering the country increased by 100 percent between 1991 and 1997, from 1.1 million to 2.2 million. The Agency's primary mechanisms to ensure that food products conform to applicable safety and sanitation laws and regulations include compliance monitoring activities, inspections, equivalency evaluations, foreign country, wharf examinations and sample collections and analyses. In addition, the Agency provides technical assistance and training, including inspector training, to help foreign nations improve their ability to ensure the safety and sanitation of imported foods.

The Agency also works with and through states to expand inspection coverage of the food supply. Under the Cooperative Programs, FDA works jointly with states to ensure the safety of milk products, shellfish, and retail foods. States conduct inspections of establishments engaged in interstate commerce under contractual agreements with FDA. In recent years, partnership arrangements have been established with states in which they agree to conduct food safety inspections that meet the Agency's regulatory specifications. Additionally, the Agency has begun working with state and local agencies and other Federal agencies, including USDA and CDC, to develop an integrated food safety system for the Nation. This system will ensure greater coverage of the food supply, more efficient use of available resources, and greater uniformity and consistency in safety standards.

Ensuring the safety of nutrition supplements is another important area of activity under this strategic goal. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, FDA is required to regulate dietary supplements as foods and to respond to companies on certain questions of labeling and other requirements. In view of the rapidly increasing use of and safety hazards associated with some of these products (e.g., ephedra), dietary supplements are a major health concern.

FDA is developing and using new and innovative approaches to respond to the increasing number and complexity of food safety issues, the rapidly increasing size of the food supply, and consumer demands for greater protection from foodborne hazards. One of these approaches is the expanded use of quality control systems (such as HACCP) that emphasize preventing food contamination. The main advantage of HACCP systems is that they permit food establishments to identify and properly control points in the process where safety or sanitation problems could occur.

FDA also uses food safety education and technical assistance as another strategy to protect consumers from foodborne hazards. These activities, which are often sponsored in conjunction with other federal agencies, states and professional associations, provide the most cost-effective means to prevent processing, preparation, handling and storage practices that could cause food to become contaminated with microorganisms or other substances that could cause illnesses. Research-based food safety education campaigns can reach large numbers of food preparers, including those in the retail sector and consumers, with information on safe food handling practices that can prevent food contamination and reduce pathogen growth. Also, through its education activities, the Agency efficiently and effectively delivers food safety messages to special populations (e.g., pregnant mothers, the elderly, and immune-compromised individuals) who are especially vulnerable to certain foodborne hazards such as microbial pathogens.

Research and risk assessment are critical and interdependent components of FDA's strategies for prevention and control of microbial pathogens and their toxic metabolites and for responding efficiently to foodborne disease outbreaks. Food safety practices and programs must be based on sound scientific research. Research must be conducted in a manner that supports the Agency's ability to perform risk assessments. Conversely, risk assessment provides a framework for assessing the relative impact of foodborne hazards and setting program priorities. Increased coordination between the risk assessment and research programs will enhance the responsiveness and cost-effectiveness of the Agency's food safety research program and thus enhance the Agency's capability to achieve its regulatory mission. Research provides the detailed information needed about each pathogen. Risk assessment uses analytic approaches that allow FDA to evaluate these pathogens and their toxins from initial production, through processing, to consumption. Critical elements are identified that focus research and lead to developing cost-effective means for lowering the risk of illness.

The international harmonization activities included under this strategic goal promote the development of science-based international standards for foods. The Agency takes a leadership role in the development of the *Codex Alimentarius* General Standard for Food

Additives and the North American Free Trade Agreement Technical Working Group (NAFTA TWG), and promotes the development of science-based international standards for foods. Also, the technical support provided in trade disputes involving the safety of food additives promotes the use of science-based international safety standards. These and other international efforts will help ensure that imported foods meet safety and sanitation standards that are comparable to those in this country.

All of the activities in this strategic goal directly benefit consumers. Compliance monitoring activities permit the Agency to reduce the risk of foodborne illness by preventing contaminated foods from entering the marketplace or quickly removing them once they are identified. Through its education and technical assistance activities, the Agency is able to provide industry and consumers information on how to prevent food safety hazards. International harmonization activities help ensure that consumers are protected from hazardous imported food products. Moreover, research and risk assessment activities of this cluster provide the information, knowledge and expertise that establish the foundation upon which the Agency must base policies, standards and regulatory initiatives to help reduce the incidence of food-related illnesses. However, public health data systems currently do not provide the data required to accurately and realistically establish ultimate outcome goals for these activities. In the next few years, it is expected that the FoodNet systems, which are active surveillance programs, will provide data adequate to establish baselines for foodborne illnesses. These baselines will permit the Agency to objectively assess the impact of its activities on the public health. (For further information, see the Verification and Validation section at the end of the Foods Program section.)

Approaches, Skills, Technology, and External Factors:

Preventive Control Systems

Partnership agreements with states and equivalence agreements with foreign countries are necessary to help FDA promptly assure that seafood products available to consumers are produced under effective HACCP-based systems. FDA has developed a national seafood HACCP inspection database to record industry compliance. Efforts are also being undertaken to explore ways to evaluate the effectiveness and benefits of the new system. In addition, the Agency will implement the HACCP regulation for the fresh juice industry.

Compliance Monitoring

Resources requested for FY 2000 for compliance monitoring will permit FDA to increase domestic establishment inspections and to expand import coverage for foods. This funding request will provide the resources needed to significantly reduce the interval between inspections in domestic food establishments that produce high risk products. High-risk products include low acid canned foods (LACF), infant formulas, heat and serve products, ready-to-eat products and other foods that do not require heating to a temperature sufficient to kill bacteria prior to consumption. The current interval between

inspections of most of these establishments is between three and four years. With the additional resources requested in FY 2000 for this strategic goal, the Agency will begin implementing a strategy that will permit it to cover the entire inventory of approximately 6,250 domestic high-risk food establishments on an average of once every one to two years. As the Agency works with states on an integrated food safety system, including additional state partnerships, it expects to reduce the inspection interval for these establishments to once every year.

To increase the effectiveness of the seafood HACCP program, the Agency will seek to transfer from the National Oceanic and Atmospheric Administration to FDA the personnel and functions of the National Seafood Inspection Program of the National Marine Fisheries Service (NMFS). NMFS' voluntary inspection program is essentially trade-oriented, but also works to obtain industry compliance with FDA's safety standards. If the Voluntary Seafood Inspection Performance-Based Organization Act is passed, it will establish the Seafood Inspection Program as a Performance-Based Organization within FDA. A Performance-Based Organization is an entity that provides necessary Governmental services for a fee, and whose activities could be enhanced by allowing it to function in a business-like manner while retaining policy direction from the Agency. The location of the PBO within FDA will help promote the efficiency and effectiveness of seafood safety activities at the federal level. This arrangement will permit closer coordination of inspectional activities, enhance uniformity in regulatory approaches and safety standards, and assure the most efficient use of resources. Under the PBO, the cost for services will be recovered through user fees paid by those who benefit from these services.

To improve the coverage for the entire food supply, FDA will use resources provided at the increased funding level to work with state and local agencies as well as USDA, CDC, and other federal agencies to establish an integrated food safety system for the Nation. On September 14 - 17, 1998, a meeting attended by 170 participants, including representatives from federal agencies and all 50 states, was held in Kansas City to explore how regulators at the federal and state levels can work together to improve the safety of foods. Such a system would ensure greater uniformity and consistency in food safety standards and may include federal oversight. A subsequent meeting on the integrated food safety system was held in December in Baltimore where work groups composed of federal and state officials were created to identify and discuss issues related to the development of an integrated food safety system. These issues included roles and responsibilities, outbreak response coordination and investigation, information sharing and data collection, minimum uniform standards and laboratory operation and coordination. In FY 2000, FDA will work with federal and state agencies to plan the implementation of an integrated food safety system. Effective coordination between all the partnering agencies and organizations involved in ensuring the safety of foods offers the best opportunity to significantly improve protection for consumers and achieve substantial reductions in foodborne illness.

Additional resources requested for this strategic goal for FY 2000 will permit the Agency to achieve a much-needed increase in the coverage of imports. With the rapid growth in

imported food products over the past decade, the level of coverage declined from 7 percent in FY 1991 to around 2 percent in FY 1997. The increase in coverage will be achieved primarily by conducting additional foreign inspections/evaluations and expanding the reviews of electronic filers. Filer reviews help the Agency detect deliberate or inadvertent miscoding of filed information on imports. For example, canned mushrooms, which are automatically detained, may be miscoded as dried mushrooms that are not automatically detained. Similarly, mixed entries may be coded as one type of food product. In other cases, firms whose products are flagged for automatic detention may use the code for another firm whose products are not detained. One goal is to increase the accuracy of import entry data electronically submitted to the FDA so that no more than 10 percent of entry lines contain an error. Since the tariff codes assigned by U.S. Customs do not identify and differentiate FDA-regulated products, FDA regroups products, forming Customs' tariff codes into "entry lines." Entry lines are individual lots of imported products, such as a truckload of canned peas, a single x-ray machine, or a boatload of bananas. In addition, resources will be available to increase the number of partnerships and MRAs with foreign nations. These international agreements permit the Agency to establish safety and sanitation standards that food products must meet before they are exported to the United States. The development of these agreements must be supported by evaluations conducted of food safety systems in foreign nations.

Education and Technical Assistance

With the additional resources provided for this strategic goal, FDA will work with states and the food industry to develop and implement food production and preventive control systems (e.g., HACCP) and establish regulatory processes and systems to more efficiently and effectively monitor the food supply. The Agency will also encourage more states to adopt the Food Code. FDA will also expand its work with other federal agencies and states to implement a national education program that ensures greater safety in retail food preparation practices using concepts set forth in the Food Code.

Research and Risk Assessment

Resources requested for this goal in the FY 2000 budget will permit FDA to expand its research efforts to fill critical gaps in its food science base. This includes developing more rapid and accurate analytical methods for detecting bacterial agents in foods, especially those that are difficult to detect, and more effective techniques to prevent and control microbial pathogens on foods. The resources provided will also allow FDA's scientists to provide more technical guidance and assistance to industry, consumers, and other constituencies. Moreover, FDA scientists will be better equipped to serve as national and international experts who provide technical expertise for the development and harmonization of international food safety specifications and standards.

The National Center for Food Safety and Technology (Moffett Center) and the Joint Institute for Food Safety and Applied Nutrition (JIFSAN) are key components of FDA's efforts to achieve established food safety objectives, especially those under the Food Safety Initiative (FSI) and Produce and Imports Food Safety Initiative (PIFSI). These

partnerships with academia and industry allow for more efficient use of research resources and enhance the quality of food safety and nutrition research and public health policy. The additional resources requested for FY 2000 will permit FDA to expand risk assessment efforts in JIFSAN and the Moffett Center to fill critical gaps in its ability to assess exposure to foodborne hazards. This expanded risk assessment research effort will enhance FDA's ability to more rapidly and accurately characterize the nature and size of the risk to human health associated with foodborne hazards, as well as the effects of intervention. More rapid and accurate risk assessment techniques are critical to Agency efforts to provide consumers greater protection against potential hazards posed by foodborne pathogens and other contaminants.

Dietary Supplements

The Dietary Supplement Health and Education Act (DSHEA) requires that companies make certain submissions to FDA when health claims are made for dietary supplements and provide a scientific basis for the safety of new dietary ingredients. Review of these submissions requires a varied collection of skills such as those of Medical Officers, Consumer Safety Officers, Chemists, Botanists, Herbalists, Toxicologists and other scientists. Notifications that are reviewed by FDA must be done within the specified time frames.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Eighty percent of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning Hazard Analysis Critical Control Point (HACCP) systems.

****This goal supports the accomplishment of the NPR High Impact Agency goal, Stronger Food Quality Assurance****

Data Sources: FDA's Field Data System; National Seafood HACCP Compliance Database System

Baseline Data:

Under development. The requisite software programs are being designed and tested to analyze the results of inspection findings.

FY 1998:

Conducted 3,876 initial HACCP verification inspections.

FY 1999:

50% of the seafood industry will be operating preventive controls for safety as evidenced by functioning HACCP systems (target).

Note about Baseline Data: Data on seafood HACCP verification inspections that are needed to establish realistic baselines for this goal will not be available until March 31, 1999. An automated computer data collection system was established to receive and record inspection findings sent from remote locations by fax machines. To assure

uniformity in determining compliance with the seafood HACCP regulation, only inspection results from HACCP trained and certified inspectors using the standardized inspection forms are accepted. Findings are given a quality control review before entry into the National Seafood HACCP Compliance Database. Once the compliance baseline is established (by 3/31/99), the performance goals for industry compliance in FY 1999-2002 will be reassessed.

Goal Statement: Increase the frequency of high-risk domestic food establishment inspections to once every one to two years, and annually beginning in FY 2001.

Data Source: Field Data Systems.

Baseline Data:

FY 1998:

Through a combination of FDA and state contract inspections, cover 25% to 33% of the 6,250 high risk food establishments

FY 1999:

Same as FY 1998 (target).

Note about Baseline Data: The existing Field Data Systems currently do not differentiate between low-, medium-, and high-risk domestic food establishments. The Agency has established a definition for high-risk establishments, which include those involved in the manufacture of low acid canned foods (LACF) products, infant formula products, heat and serve products, ready to eat products and other foods that do not require heating to a temperature sufficient to kill bacteria prior to consumption. Based on this definition, the Agency estimates that there are approximately 6,250 such establishments in its establishment inventory. It also estimates that these establishments are currently inspected on average once every three to four years. Beginning in FY 2000, the number of high-risk establishment inspections conducted annually will be increased to at least half of the inventory (approximately 3,125 establishments). As work progresses on this goal, better distinctions will be made between high-risk and the medium and low-risk inspections, and more accurate information will be obtained regarding the actual number of high-risk establishments. This information, along with annual inspection accomplishments, will provide the basis for establishing an accurate baseline for high-risk inspections.

Goal Statement: Assure that FDA inspections of domestic food establishments,⁽²⁾ in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.

Data Source: Field Data Systems

Baseline Data:

FY 1997:

98%

FY 1998:

98%

FY 1999:

at least 90% (target)

Note about Goal: Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector.

Goal Statement: Initiate Hazard Analysis Critical Control Point (HACCP) systems in the juice industry.

Data Source: Field Data Systems.

Baseline Data: Baselines for juice HACCP will be established based on the inspection data collected and analyzed during the first year of implementation.

FY 1998:

Publish a proposed regulation for juice HACCP and evaluate comments.

FY 1999:

Publish a final rule and prepare to implement the juice HACCP regulation by providing training, technical assistance, guidance and other assistance to industry and states.

Note about Baseline Data: A target for this goal describing the percentage of the industry to be covered will depend on the final rule and the date on which the verification process is initiated. Based on experience in implementing HACCP in the seafood industry, the sequence of milestones to be reached in the implementation of HACCP in the juice industry will include reviewing public comments on the proposed rule; finalizing the rule; meeting with industry to explain the new rule, how they can implement it, and what the elements of a good HACCP plan are; publishing a document similar to the seafood "Bad Bug" book; developing guidance for state partnerships to conduct juice HACCP inspections; and providing technical assistance to industry before and after verification inspections.

Goal Statement: Continue to develop and implement voluntary guidance and other efforts to improve the safety of fresh fruits and vegetables, and work with USDA to

conduct a 1999-2001 National Agricultural Statistics Survey (NASS) of microbial contamination of fresh produce to collect the data required to evaluate program effectiveness.

Data Source: NASS survey for 1999-2001 for fresh fruits and vegetables.

Baseline Data:

FY 1998:

Conduct grassroots meetings on GAP and GMP guidance with domestic and foreign fresh produce growers, producers, processors and manufacturers. Issue broad-scope guidance on GAPs/GMPs for growers and producers of fruits and processors of fresh produce.

FY 1999:

Complete a pretest of the survey instrument by early FY 1999. Assuming OMB approval under the Paperwork Reduction Act, surveys will be conducted in New York State and California covering 20 of the most-consumed fruit and vegetables.

Note about Baseline Data: The raw data for establishing baselines for these products are expected to be available in FY 2000. Current plans include the ongoing development and implementation of surveys to cover produce from other states. In addition, survey questions are being designed so they can be used in surveys of produce operation in foreign countries.

Goal Statement: Increase the number of inspections/evaluations of foreign food establishments from 100 to 250.

Data Sources: Field Data Systems and surveys.

Baseline Data:

FY 1998:

Conducted 43 foreign inspections/evaluations.

FY 1999:

Conduct approximately 75-100 foreign inspections/ evaluations (target).

Goal Statement: Achieve adoption of the Food Code by at least 35 percent of the states.

Data Source: Field Data Systems

Baseline Data:

FY 1997:

Three states (6%) adopted the Food Code.

FY 1998:

Ten states/jurisdictions (20%) reported adopting the Food Code.

FY 1999:

Achieve adoption of the Food Code by 13 (25%) of the states (target).

Goal Statement: Develop modeling techniques to assess human exposure and dose-response to certain foodborne pathogens, the potential risk for those pathogens causing human illness, and the setting of safety performance standards to regulate microbial content of food towards reducing incidence of foodborne disease.

Data Source: Periodic modeling techniques and peer reviews.

Baseline Data:

FY 1999:

There are no generally agreed-upon modeling techniques to assess human exposure and dose response to foodborne pathogens and the potential risk of human illness. The development of modeling techniques will result in more rapid and accurate evaluation of risks associated with bacterial pathogens and will help FDA establish research and regulatory priorities.

FY 2000:

Conduct a quantitative microbial risk assessment of a pathogen/food pair that represents a current food safety issue such as *Vibrio parahaemolyticus* in molluscan shellfish and *Listeria monocytogenes* in raw or ready-to-eat foods.

Goal Statement: Develop and make available an improved method for the detection of hepatitis A virus, *Cyclospora cayentanensis* and *Escherichia coli* O157:H7 on additional fruits and vegetables, and provide knowledge and technologies needed to develop guidance and methods for the control and elimination of pathogens on particular fruits and vegetables such as *Escherichia coli* O157:H7 and *Salmonella spp.* from juices, leafy vegetables and sprouted seeds and *Cyclospora* from soft fruit (e.g., berries).

Data Sources: Periodic management and peer reviews.

Baseline Data:

FY 1998:

Developed and began implementing an interagency research plan that more effectively coordinates the food safety research activities in FDA and USDA.

FY 1999:

Continue efforts to implement research projects in the interagency research plan that are designed to develop more rapid and accurate methods for detecting bacterial contaminants on fresh produce. Traditional analytical techniques often do not work well in fresh produce because of interference from natural constituents in these products. Therefore, these activities are essential to Agency efforts to provide consumers a greater level of protection against these potential food safety hazards.

Goal Statement: Develop more rapid and accurate analytical methods for foodborne chemical contaminants (including bacterial toxins).

Data Sources: Periodic management and peer reviews and progress on the interagency research plan developed with USDA.

Baseline Data:

Baseline data do not currently exist for these research activities. This research supports the program's compliance monitoring, regulatory, education and other activities to improve the safety of the food supply. Using the results of these research efforts, FDA will be able to respond more effectively to hazards posed by foodborne contaminants, including bacterial toxins and newly identified food safety hazards such as naturally occurring toxin constituents.

Strategic Goal 3:

Provide the type, amount and quality of intelligence on food-related injuries and causative agents to permit the Agency to better target policy development and research activities to food safety problems of the greatest public health significance.

Resources: \$11,026,000 90 FTEs

Performance Goals:

- Establish an integrated adverse event reporting system for food and cosmetic products, with emphasis on increasing efforts to design and implement modules needed to record dietary supplement adverse event information.
- Work with the Centers for Disease Control and Prevention (CDC), the U.S. Department of Agriculture (USDA), and states to increase food safety surveillance and to improve responses to foodborne illness outbreaks.

Rationale:

Accurate and comprehensive intelligence on foodborne illnesses and their causes is essential to the development and implementation of effective strategies to protect consumers. While a number of systems provide information on narrow aspects of food safety, no public health data systems provide the amount and types of accurate and comprehensive data required to better understand foodborne illnesses and the substances that cause them. FDA is working internally and in conjunction with other agencies and states to develop better foodborne illness data.

In FY 1995, FDA and USDA began working with CDC to improve foodborne illness surveillance activities. FoodNet is a major product of this cooperative venture. FoodNet 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 partners link illnesses that have a common cause, no matter where they occur. In a related project, FDA is working in concert with CDC and the Conference of State and Territorial Epidemiologists (CSTE) to improve the forms used by state and local authorities to report on foodborne outbreaks of illness and injury.

FDA, USDA, and CDC are also cooperating in PulseNet, a computer-supported network that will compare deoxyribonucleic acid (DNA) fingerprints of microbial isolates from patients and from food products anywhere in the farm-to-table continuum. Although still in the start-up stage, this system has already proved valuable in linking and speeding trace-backs of illnesses caused by *E. coli* O157:H7 contamination in sprouts, lettuce, and cheese curds. When fully implemented, PulseNet will permit illness investigations to more accurately pinpoint specific products and even sources of raw materials for the products that are implicated in illness outbreaks. This capability will permit FDA and USDA to save time and resources in conducting trace backs to determine the source of foodborne contaminants.

A Foodborne Outbreak Coordination Response Group (FORCG) was established to evaluate the effectiveness of current response procedures in large outbreaks that involve several agencies, and to assure better federal-state-local coordination of the evaluation and response to foodborne illness. FORCG is composed of representatives from FDA, CDC, USDA, Environmental Protection Agency (EPA), Association of Food and Drug Officials, CSTE, and several other organizations. This group is currently working with state health organizations to help them understand its foodborne illness information needs.

FDA has a number of other systems that provide information on food and cosmetics-related injuries. These include the Adverse Reaction Monitoring System that contains consumer complaints of illness and injury from food products regulated by FDA. The Cosmetic Adverse Reaction Monitoring program is the principal way that the Agency obtains information about harmful cosmetic products. The National Health and Nutrition Examination Survey, which is funded by FDA, CDC, and the National Center for Health Statistics, is another system that provides valuable information on the nutrient status of the American public that may be used in assessing the effectiveness of nutrition activities, initiatives and programs.

The Agency has a critical need at this point to improve the timeliness and accuracy of the reporting of adverse events associated with food and cosmetic products. In order to meet this need, FDA must expand efforts to develop and maintain a modern and responsive system to receive, store, manipulate and report out information on adverse events, especially those associated with dietary supplements. Recent experiences with ephedra and cases of serious injury including deaths associated with other dietary supplements underscore this need. Dietary supplements, including vitamins/minerals, botanicals, amino acids, glandulars, and other naturally occurring compounds, are not subject to premarket review and approval by FDA before they are marketed. Therefore, information on patterns of usage, target populations of those most vulnerable to adverse reactions and

other relevant data are critical to efforts to improve the protection provided consumers against potentially hazardous dietary supplement products.

Systems that provide better intelligence on food and cosmetic safety hazards, the types of contaminants that cause them, and information on changes in food consumption behaviors and attitudes ultimately benefit consumers in several ways. First, they provide the information required to more rapidly and accurately identify and respond to products that pose a potential risk to consumers. Each day saved in responding to an illness outbreak can prevent thousands of illnesses and save many lives. Second, better foodborne illness data permit the Agency to develop and focus regulatory strategies to prevent foods from becoming contaminated. Third, with better information about illnesses associated with food and cosmetic products, the Agency can focus research, education campaigns and other activities where the greatest food safety problems exist. Finally, these data systems will provide the information needed to establish realistic outcome measures that will permit FDA to evaluate the effectiveness of its programs to promote and protect the public health more objectively and become more accountable to Congress and consumers.

Approaches, Skills, Technology, and External Factors:

The FDA must maintain and increase its human resources and skills in epidemiology, statistics, molecular microbiology, federal/state cooperation, and international cooperation. In each of these areas, the skills will be leveraged through cooperation with other agencies and state officials. Many FDA officials will also invest time to learn to use the new, more complex and more informative injury reporting results. Additionally, more FDA laboratory experts will be trained in and equipped with the newest methods of molecular subtyping of pathogenic microbes.

The additional resources requested for this strategic goal will permit FDA to work with USDA, CDC and states to expand foodborne outbreak response and traceback activities. These resources will be used to increase involvement of state public health officials in the process and establish an electronic system to promote more efficient communications among the states and other involved agencies. Also, the Agency will develop more effective practices and procedures for illness outbreak coordination and work to build a strong, cooperative approach to ensure more rapid response to outbreaks of foodborne illness.

FDA will also use the additional resources requested for FY 2000 to develop the capability to deal more effectively with the ever-increasing number of reported adverse events associated with food and cosmetics products. Emphasis will be placed on improving adverse events reporting for dietary supplements. Specifically, the increased resources will be devoted to the following:

- Enhancement and implementation of an integrated adverse events reporting system that is compliant with the Agency's ISA standards and designed as a potential module for a larger Agency-wide system.

- Improvement of automated reporting, including electronic access through the World Wide Web.
- Improvement of records management procedures to meet the increasing volume of electronic and other FOI requests for adverse events reporting for dietary supplements.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Establish an integrated adverse event reporting system for food and cosmetic products, with emphasis on increasing efforts to design and implement modules needed to record dietary supplement adverse event information.

Data Sources: Integrated Agency Science-Based Reporting, Monitoring, and Evaluating Adverse Events System.

Baseline Data:

The requisite hardware and software systems need to be purchased for integration of current Center-based systems with limited capacity.

Goal Statement: Work with the Centers for Disease Control and Prevention (CDC), the U.S. Department of Agriculture (USDA), and states to increase food safety surveillance and to improve responses to foodborne illness outbreaks.

Data Sources: The FoodNet Surveillance System and PulseNet System

Baseline Data:

FY 1998:

Expand the demographic diversity and size of the population covered by FoodNet by increasing the number of 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 illness outbreaks.

FY 1999:

Continue FoodNet and add more states to PulseNet.

Strategic Goal 4:

Reduce diet-related diseases by providing consumers adequate and accurate information on the nutrition content of foods, reduce injuries related to safety hazards in cosmetic products, and prevent food related economic fraud.

Resources: \$9,800,000 97 FTEs

Performance Goals:

- Increase to at least 55 percent the proportion of adults who report changing their decision to buy or use a food product because they read the food label.
- Maintain the restored level of activity for cosmetic voluntary reporting to protect consumers against potentially hazardous cosmetic ingredients or products.

Rationale:

This goal includes food labeling, cosmetic and economics activities. The food label and associated labeling is the food producer's primary tool to provide information to the consumer concerning nutritive value, ingredients and information on safe handling and use. FDA's authority over the content of the food label extends to over 260,000 classes of food products with about 10,000 new products appearing on grocery shelves each year. Cosmetic activities include compliance monitoring and follow up to cosmetic injury reports. These activities are critical to Agency efforts to ensure the safety of cosmetics since there is no premarket approval requirement for either cosmetic products or their ingredients, except colors. The Agency's food economics activities protect consumers from products that are fraudulent.

Major food labeling objectives are: 1) improve the nutritional quality of the American diet and 2) provide information for the safe consumption of food. Recent information has demonstrated the significance of a healthy diet for the overall health of the consumer. Additionally, the label can serve as an important medium for providing the consumer with information on ingredients of food, including allergens and other substances that cause adverse reactions, as well as cautionary information on food handling, such as the need to promptly refrigerate foods.

Because unsafe cosmetics pose a risk to public health, it is critically important that FDA take prompt and effective steps to find unsafe products and remove them from distribution. The burden is on the Agency to find harmful products and develop the data necessary to support legal action. Under these circumstances, consumers may be exposed to a public health hazard that is difficult to detect, especially when the effect is subtle and/or not easily associated with use of the product. FDA protects public health mainly through monitoring the marketplace and through enforcement of cosmetic regulations. These activities ensure that appropriate actions are taken to find and remove unsafe products from the marketplace and to prevent problems before they occur.

FDA's role in preventing economic deception is essential in maintaining consumer confidence in marketed food products. The primary objective is to reduce the potential for economic adulteration through the use of cheaper ingredients and to ensure that consumer expectations are consistently met on subsequent purchases of the same commodity food item. Industry stakeholders have requested that FDA revise food standards to make them more flexible in accommodating newer technologies and more healthy ingredients. In addition, agencies such as the Food and Nutrition Program of USDA rely on FDA Standards of Identity to set specifications for its School Lunch and Special Supplemental Food for Women, Infants and Children (WIC) programs.

The activities in this goal benefit consumers by ensuring that food labeling is useful and accurate, that cosmetics are safe, and that foods represent the value they purport to deliver. Food labeling provides consumers the nutritional information needed to make healthy food choices that help prevent diet-related diseases such as heart conditions, strokes and certain cancers. Also, ingredient labeling provides valuable information for those who need to avoid certain food components, especially foods that may cause an allergic reaction. FDA's cosmetic program is the consumer's primary regulatory protection against hazardous cosmetic products or ingredients. While the economic issues do not present a public health hazard, they do help consumers assure that the foods they buy represent a fair value. As is the case with the other goal areas for food safety, these benefits cannot be quantified in outcome performance measures. This is primarily because data systems do not currently exist to provide the types and amounts of data required to establish and verify baselines.

Approaches, Skills, Technology, and External Factors:

Food Labeling

Currently, there are no collaboratively studied methods for measuring nutrition components, such as total *trans* fatty acids or conjugated linoleic acids, in food products. Also, current methods for measuring total dietary fiber in foods exclude a number of fiber components that appear to have beneficial effects. Research related to food labeling activities focus primarily on assuring the availability of accurate and efficient analytical methods for measuring the nutrients present in food products.

Clear labeling policies and provisions need to be implemented to better protect the consumer from adverse reactions, including serious reactions that could be a threat to life. These policies should ensure that food labels adequately inform consumers of the presence of allergens and other substances that may cause adverse reactions. In addition, consumers have asked the Agency to develop a strategy that can be used for disseminating such information to consumers in restaurants and food service establishments. It is also critically important that FDA take measures to assure that the public understands how to use the label as a dietary tool to a much greater extent than presently exists. Understanding how to use the food label effectively represents a major opportunity for the government to empower consumers with the ability to make choices that will help prevent chronic and acute diseases caused or exacerbated by poor nutrition.

Cosmetics

Cosmetic enforcement and regulation require a thorough knowledge of cosmetic law, regulations, past precedent actions and known product safety issues. It also requires a thorough knowledge of procedures and effective interaction with responsible field offices, other FDA centers, FDA general counsel, laboratory support, outside experts, states, and individual companies to pursue Agency actions against violative products.

Cosmetic enforcement and regulation activities are critical to implementing program initiatives through the field offices and preparation of guidance documents. For example, this project is responsible for preparation and coordination of the field work plan for monitoring cosmetic manufacturers for their use of bovine ingredients and ensuring that U.S. consumers are protected from exposure to the bovine spongiform encephalopathy (BSE) infectious agent.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Increase to at least 55 percent the proportion of adults who report changing their decision to buy or use a food product because they read the food label.

Data Sources: FDA Health and Diet Surveys.

Baseline Data:

FY 1990:

In FY 1990, the Health and Diet Survey (pre-NLEA) found that 30% of adults used the food labels to make a decision on the purchase or use of food products.

FY 1995:

Data from the 1995 survey disclosed that 48% of people age 18 and older reported changing their decision to buy or use a food product because they read the food label.

FY 2000:

The next Health and Diet Survey will include FDA's tracking questions related to food labeling.

Goal Statement: Maintain the restored level of activity for cosmetic voluntary reporting to protect consumers against potentially hazardous cosmetic ingredients or products.

Data Sources: Voluntary reporting information for cosmetic establishments and product formulations submitted to FDA by cosmetic product manufacturers, packers and distributors

Baseline Data: FDA suspended operation of the cosmetic voluntary reporting program in March 1998 due to budget shortfalls. The database has been maintained since it was suspended but has not been updated with any new submissions. In FY 1999, the Agency will work with the regulated industry to update the database for voluntary reporting. The updated database will provide the information required to establish an accurate baseline for this activity.

Verification and Validation

Public health data systems currently are not adequate to provide accurate and comprehensive baseline data needed to draw direct relationships between FDA's regulatory activities and changes in the number and types of foodborne illnesses that occur annually in this country. Because of the need to have better data on food related illnesses, FDA and USDA began working with CDC in 1995 to improve food safety surveillance. FoodNet, an active surveillance program, was created through this joint effort. Currently, there are seven FoodNet sites and another one will be added this year.

These sites, which operate in areas that are representative of the geographic and demographic population distributions in this country, provide much better data on the number of foodborne illnesses and trends in terms of the types of contaminants that are causing these illnesses. This type of information can be critical to efforts by food safety agencies to redirect their regulatory and research resources to those food safety problems that pose the greatest threat to the health of consumers. Moreover, in 2002 when the data will be sufficient in volume and quality to establish baselines against which to measure changes in foodborne illnesses, FDA will be in a better position to establish broad scope outcome goals that are essential to effective performance planning.

Food Safety regulation development and research activities are planned and tracked through internal management systems. Progress on the development of regulations is tracked mainly through CFSAN's document tracking system and the *Federal Register* document tracking system. These systems permit the Agency to track the processing of regulations from the time they are filed to the point at which action is complete--usually the publication of a final regulation in the *Federal Register*.

CFSAN uses a number of internal data systems to track premarket review progress. These include the Management Assignment Tracking System (MATS) to track progress of petition reviews, Correspondence Tracking System (CTS) to track progress on biotechnology consultations, and internal databases to track biotechnology consultations, and reviews of GRAS notifications, nutrient content claims, and health claims petitions/notifications. Outcome-oriented performance information can be extracted from MATS only by a labor-intensive manual process. CFSAN's internal data systems are limited to tracking time to a completed review and do not have the capability to track distinct phases of the review process. In FY 1998, the internal OPA database will be modified to permit more detailed tracking of CFSAN's action on biotechnology consultations. In FY 1999, CFSAN will implement an electronic workflow system that will replace MATS and CTS and permit real-time monitoring of review progress. The electronic workflow system is expected to be in full use in FY 2000. This new system will automatically track actions related to the processing of food and color additive petitions, GRAS petitions and biotechnology consultations.

FDA uses a variety of data systems to develop and verify performance goals for its safety activities. Among these are several field data systems. The most important of the field data systems are the Program Oriented Data System (PODS) and the Operational

Administrative System for Imports (OASIS) . PODS tracks field activities conducted by FDA's field force and the firms over which FDA has legal responsibility. Information provided by this system includes data on the number of inspections, wharf examinations, and sample collections and analyses as well as the time spent on each. OASIS, which is coordinated with the U.S. Customs Service , provides data on what products are being imported as well as where they are arriving. It also provides information on compliance actions related to imports. By FY 2000, the Field Accomplishments Tracking System (FACTS) will replace PODS as the primary mechanism for tracking compliance activities for the domestic food industry. The National Seafood HACCP Compliance Database System maintains information on seafood HACCP inspections conducted by FDA and States under partnership with FDA. Standardized forms (Cardiff forms) are used to assure comparability of HACCP compliance data whether the inspections are conducted by FDA or the states. Another field data collection instrument is the field survey. Field surveys are special assignments that are developed and implemented specifically to collect information needed to more thoroughly evaluate the nature and extent of particular postmarket food safety problems.

Data are also gathered through a number of other surveys designed for specific purposes. These include the Health and Diet Survey that provides information required to evaluate the impact of the Agency's food labeling activities. These surveys include questions that are designed to query consumers on how they use food labeling information to make decisions to use or purchase food products. Another survey is the NASS survey currently being developed jointly by FDA and USDA to evaluate the impact of GAPs and GMPs for improving the safety of fresh fruits and vegetables. The survey questions will be designed to provide data on practices employed in the production and processing of fresh fruits and vegetables. The results of the NASS surveys will be used to establish baselines for industry practices as well as evaluate the impact of voluntary GAPs and GMPs on improving production and processing practices for fresh produce.

Comprehensive data on illness caused by food and cosmetic products are critical to efforts to protect the health of consumers. Some of the illness data are provided by databases that contain information on adverse events, reported by consumers and industry on food and cosmetics products. In FY 2000, the Agency will improve the quality of data on adverse events through the development and implementation of an integrated adverse event reporting system.

Proposed research projects are subjected to management reviews prior to implementation and periodic management reviews after the projects have been initiated. The primary planning and management system for food safety research is the Center Program Resources (CPR) plan system which provides quarterly resource use reports and semi-annual reports on accomplishments versus planned milestones. In addition, research projects are subjected to periodic external peer reviews. Peer reviews by recognized scientific experts in various disciplines related to food safety provide objective feedback that helps FDA evaluate the progress, quality and relevance of its research activities. In addition, risk assessment models are verified periodically using statistical models that

assess their ability to make rapid and accurate estimates of risks associated with a particular food safety hazard.

PulseNet is another data system that will be critical to federal and state efforts to provide greater protection for consumers. PulseNet is being developed and implemented jointly by CDC, FDA, USDA, and states. Using this new system, participating public health laboratories anywhere in the Nation can share information on the distinctive fingerprinting patterns of a pathogen that is causing illness. This will permit public health officials to determine quickly whether a widespread food borne illness outbreak is underway. If the information indicates that there is a widespread food safety problem, action can be taken to remove quickly potentially hazardous products from the marketplace and conduct tracebacks that can rapidly and effectively identify the source of the contamination.

1. Achievement of this performance goal target level is dependent upon passage of User Fee legislation and establishment of management systems to implement user fees by the beginning of FY 2000.
2. Excludes domestic seafood establishments.

HUMAN DRUGS

Total Program Resources (FY 2000):	\$000	FTEs
Center	245,996	1,733
Field	70,764	832
Total	316,760	2,565

Program Overview

The Human Drugs Program assures that all drug products for the prevention, diagnosis, and treatment of disease are safe, effective and properly labeled. The Prescription Drug User Fee Act (PDUFA) of 1993, reauthorized for another five years by the FDA Modernization Act of 1997 (FDAMA), provided the impetus that allowed the Agency to cut approval times for new drugs nearly in half while doubling the number of drugs approved. Americans now have faster access to new therapies, suffer less, recover more rapidly, and live longer lives, or enjoy an improved quality of life. The Human Drugs Program will continue to pursue strategies that streamline the drug development process and continue to lower median total approval time for new drug approvals.

As the number of drugs increase and development and review times shorten, safety issues grow increasingly complex and important. There is continuing focus on injury reporting. A completely electronic submission and review environment is targeted for 2002. International harmonization efforts demonstrate that we will reach agreement on having

the same new drug review documents submitted to the regulatory authorities of Europe, Japan and United States by the turn of the century. Collaborative efforts with academia, industry, professional societies and health care organizations are making progress toward the promise of finding scientifically sound ways of expediting drug development and making it easier to take advantage of newer technologies.

Program Strategic Goals

Strategic Goal 1:

Reduce human suffering and enhance the quality of the public health by providing quicker access to important, lifesaving drugs, and assure to the American public the availability of safe and effective drugs.

Resources: \$198,780,000 1,855 FTEs

Performance Goals:

- Review and act on 90 percent of standard original New Drug Application (NDA) submissions within 12 months of receipt (50 percent within 10 months); and 90 percent of priority original NDA submissions within 6 months.
- Provide written responses to industry within 14 days of receipt on 80 percent of formal meeting requests; make meeting minutes available to sponsors within 30 calendar days for 80 percent of meetings; and ensure that 80 percent of Type A meetings are scheduled within 30 calendar days of receipt of the meeting request, Type B meetings within 60 calendar days of receipt of meeting request, and Type C meetings within 75 calendar days of receipt of meeting request.
- Establish the capability and capacity to receive and archive Abbreviated New Drug Applications (ANDAs) submitted electronically.
This goal supports the accomplishment of the NPR High Impact Agency goal, More Efficient Drug Development
- Process 75 percent of all review documents by implementing an Electronic Document Management System (EDMS) throughout new and generic drug review divisions.
This goal supports the accomplishment of the NPR High Impact Agency goal, More Efficient Drug Development
- Increase the average monthly number of actions (approvals, tentative approvals, not approvals and facsimile requests) completed on Abbreviated New Drug Applications (ANDAs) by 3.2 percent from the FY 1997 level.
- Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and 90 percent of priority efficacy supplements within 6 months of receipt.

Rationale:

American consumers expect that they will have timely access to new drugs that are safe and effective. The pace of premarket approvals for drugs significantly picked up after

Congress authorized additional resources through the Prescription Drug User Fee Act (PDUFA) of 1992. In the new drug review program, 39 new molecular entities (NMEs) were approved, the second highest total for these important new medicines. The median total time to approval of NMEs was 13.4 months, the most rapid ever. American consumers were the first in the world to have access to more than half of these drugs. Streamlining efforts have paid off in over-the-counter and generic drug reviews as well. Despite a growing workload, a shrinking staff, and the absence of user fees, the generics program approved a remarkable 431 products in 1997--a record for the 1990s--while reducing time to approval from 39.6 months to 19.3 months over the last five years. The projected goals reflect the Agency commitment to meeting its legislatively-mandated requirements; however, actual performance has exceeded this commitment. These shortened times assure the American public faster access to needed therapies. A close working relationship between industry and the Agency also decreases review time. This is reflected in a goal that focuses on a time frame to establish meetings. However, our successes in streamlining drug reviews have unmasked other concerns that Americans have with their medicines. As the number of drugs increase and development and review times shorten, safety issues grow increasingly complex and important.

Approaches, Skills, Technology and External Factors:

Approaches to achieving this goal include project management initiatives which are contributing to increased efficiency and streamlining of the drug review process. Additionally, the Collaboration on Drug Development Improvement (CDDI) evaluates current and new approaches to substantially improve the efficiency of the drug development and assessment processes by reducing unnecessary studies and activities, increasing useful information, and improving resource utilization and shortening development times.

Also being developed are feedback mechanisms, such as formalized round tables, to involve the public, health professionals, Congress, and industry to address changing public health needs, and to establish priorities for early and continuous involvement with drug development in all therapeutic areas.

Leadership programs such as the Center for Drug Evaluation and Research Fellows Program and the Reviewer Career Path are designed to foster and develop leadership skills of selected fellows to provide a career path that is professionally satisfying and scientifically meaningful for outstanding CDER reviewers.

Technological influences include an ever-changing computer industry, increased use of information technology (IT) by the pharmaceutical industry, computer technology-specific mandates, and challenges related to communications and standards as FDA addresses IT issues that cross all of the Agency's organizations. To continuously improve the efficiency of the drug review process in a time of changing environmental influences, we must find less expensive and more efficient ways to process information. For instance, the Electronic Document Management System (EDMS) will provide for the creation, electronic signature, routing, and archival of internally generated review

documents, thereby reducing the administrative burden on reviewers and allowing them more time to spend on higher-value scientific review activities.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Review and act on 90 percent of standard original New Drug Application (NDA) submissions within 12 months of receipt (50 percent within 10 months); and 90 percent of priority original NDA submissions within 6 months.

Data Sources: Center-wide Oracle Management Information System (COMIS); New Drug Evaluation Management Information System (NDE/MIS)

Baseline Data:

FY 1996:

Not tracked prior to FY 1997

FY 1997:

100% of those acted on (some pending, not overdue)

FY 1998:

100% of those acted on (some pending, not overdue)

Goal Statement: Provide written responses to industry within 14 days of receipt on 80 percent of formal meeting requests; make meeting minutes available to sponsors within 30 calendar days for 80 percent of meetings; and ensure that 80 percent of Type A meetings are scheduled within 30 calendar days of receipt of the meeting request, Type B meetings within 60 calendar days of receipt of meeting request, and Type C meetings within 75 calendar days of receipt of meeting request.

Data Sources: Industry Meeting Tracking System: System tracks scheduling and conducting of formal meetings between CDER staff and those outside CDER requesting such meetings.

Baseline Data: To be established 10/1/99: Parameters will be established for the new reports which show performance relating to PDUFA goals and provide necessary day-to-day management of the process. The reports will be in place by early FY 1999.

Goal Statement: Establish the capability and capacity to receive and archive Abbreviated New Drug Applications (ANDAs) submitted electronically.

****This goal supports the accomplishment of the NPR High Impact Agency goal, More Efficient Drug Development****

Data Sources: CDER Electronic Document Room records

Baseline Data:

FY 1998:

Public comments on the industry guidance for the full NDA are resolved.

FY 1999:

All NDAs submitted electronically can be received and archived; industry guidance for electronic ANDAs is published for public comment; a pilot is conducted with up to 25 ANDAs submitted electronically.

Goal Statement: Process 75 percent of all review documents by implementing an Electronic Document Management System (EDMS) throughout new and generic drug review divisions.

This goal supports the accomplishment of the NPR High Impact Agency goal, More Efficient Drug Development

Data Sources: CDER Division Files System statistics

Baseline Data:

FY 1998:

Target 25% of review documents processed using EDMS

FY 1999:

Target 50% of review documents processed using EDMS

Goal Statement: Increase the average monthly number of actions (approvals, tentative approvals, not approvals and facsimile requests) completed on Abbreviated New Drug Applications (ANDAs) by 3.2 percent from the FY 1997 level.

Data Sources: Center-Wide Oracle Management Information System (COMIS), Abbreviated New Drug Application Management Information System (ANDA/MIS) and the Center for Drug Evaluation and Research - Office of Generic Drugs Quantitative Report

Baseline Data:

FY 1997:

Average monthly number of actions (approvals, tentative approvals, not approvals and facsimile requests) completed on ANDAs equals 113.

FY 1998:

114 (target)

FY 1999:

115 (target)

Goal Statement: Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and 90 percent of priority efficacy supplements within 6 months of receipt.

Data Sources: Center-Wide Oracle Management Information System (COMIS), New Drug Evaluation Information System (ANDA/NDE)

Baseline Data:

FY 1996:

Not tracked prior to FY 1997

FY 1997:

100% of those acted on (1 still pending, not overdue)

FY 1998:

100% of those acted on (some pending, not overdue)

Strategic Goal 2:

Prevent unnecessary injury and death to the American public caused by adverse drug reactions, injuries, medication errors and product problems.

Resources: \$46,592,000 126 FTEs

Performance Goals:

- Expedite processing and evaluation of adverse drug events through implementation of the Adverse Events Reporting System (AERS) which allows for electronic periodic data entry and acquisition of fully coded information from drug companies.
- Make new drug approval information increasingly available and targeted and promoted to specific user groups, such as consumers, patients, health-care practitioners and industry via the Internet, resulting in a decrease in serious medication errors.
This goal supports the accomplishment of the NPR High Impact Agency goal, Better Medical Product Information
- Develop partnerships with eight national organizations to disseminate educational information to consumers about choosing the right medications, taking medications correctly and reporting adverse reactions.
This goal supports the accomplishment of the NPR High Impact Agency goal, Better Medical Product Information

Rationale:

An estimated 1.3 million Americans are unintentionally injured each year through medical errors. The Agency received 254,841 reports of suspected drug-related adverse events in 1997. The average number of reports received has increased to more than 175,000 per year in the last five years from about 75,000 per year in the previous five years. Drug-related injuries and deaths can be reduced by maximizing the safety of medical products; developing integrated science-based systems for the reporting, monitoring, and evaluation of adverse events and product problems; and creating a more educated public. One important tool is research that will lead to better understanding of drug interactions and metabolism. Potential outcomes from this research include improved communication among the public, health professionals and the FDA about

product problems; greater assurance that problem medical products will be identified and corrective action taken; and more proactive, systematic feedback to the health care community and the public. Another important tool is to create a more educated public through expanded outreach activities and collaborative efforts with academia, professional societies and health organizations.

Approaches, Skills, Technology and External Factors:

To achieve this goal there will be a multi-pronged effort. First is increased outreach (communication, education, training) to health care professionals, industry, and the public. Partnerships will be developed with national organizations to disseminate educational information to consumers about choosing the right medications, taking medicines correctly and reporting adverse reactions. The chosen organizations have similar interests and goals as CDER along with current outreach programs to consumers and professionals. Second are collaborative research projects to understand the keys to recognition and reporting of adverse events and user error problems and communication of risk information. Finally, CDER will expand its efforts to share information within the Agency, and with other government agencies, agency stakeholders, and other relevant groups. To ensure more systematic and timely feedback, a need exists to create a national database on adverse events, medication errors, and product defects that serves the needs of FDA, health professionals, academia, and industry professionals.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Expedite processing and evaluation of adverse drug events through implementation of the Adverse Events Reporting System (AERS) which allows for electronic periodic data entry and acquisition of fully coded information from drug companies.

Data Sources: Adverse Events Reporting System

Baseline Data:

Current: Pilot, uncoded only. Periodic reports only.

FY 1998:

Pilot, five firms electronic entry, uncoded only. Periodic reports only.

FY 1999:

50% of top 15 drug companies electronically submitted, half of that group coded using International Conference on Harmonization (ICH) Medical Dictionary for Regulatory Activities (MedDRA) terminology, begin expedited report entry.

Note about Goal: By the end of FY 2000, CDER is seeking through targeted outreach efforts to have 75 percent of top 15 drug companies submitting electronically, with 50 percent of that group using MedDRA terminology.

Goal Statement: Make new drug approval information increasingly available and targeted and promoted to specific user groups, such as consumers, patients, health-care practitioners and industry via the internet, resulting in a decrease in serious medication errors.

****This goal supports the accomplishment of the NPR High Impact Agency goal, Better Medical Product Information****

Data Sources: Approval Letter for new and generic drugs and the Labeling Text or Final Printed Label (FPL) for new drugs; Process of generating and posting the Approved Labeling Text or FPL; Consumer Drug Information Sheets for NMEs; Availability of FDA's review of new and generic drugs via the internet; Prescribing Information Sheet for NMEs.

Baseline Data:

As of March 1998:

CDER web site users: 115,273

Number of page hits/accesses: 2,250,574

70% of approval letters posted in 15 days

90% of approval letters posted in 30 days

Most reviews not posted

Zero NME consumer drug information sheets

Zero prescribing information sheets

Goal Statement: Develop partnerships with eight national organizations to disseminate educational information to consumers about choosing the right medications, taking medicines correctly and reporting adverse reactions.

****This goal supports the accomplishment of the NPR High Impact Agency goal, Better Medical Product Information****

Data Sources: Number of partnerships; number of people we are reaching based on those partnerships (distribution lists, partners' constituents, organizational members, mailing lists)

Baseline Data:

FY 1998:

Two national organizations working with CDER as partners to develop initiatives and disseminate information.

FY 1999:

Four national organizations working with CDER as partners to develop initiatives and disseminate information.

Strategic Goal 3:

Protect consumers by assuring the ongoing availability of high quality drugs.

Resources: \$71,388,000 584 FTEs

Performance Goals:

- Develop a list of bulk drug substances that may be used in compounding and publish a rule to be used for pharmacy compounding.
- Complete 25 percent of the research projects started in FY 1999 under the auspices of the Product Quality Research Initiative (PQRI), a collaboration among FDA, industry and academia established to provide a scientific basis for policy and guidance development in the Center for Drug Evaluation and Research (CDER) on issues of drug product quality and performance.
- Complete 75 percent of research projects identified in the Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) designed to develop rational, scientific-based requirements for drug substances, drug products and excipients to ensure a high standard of drug product quality and product performance for making regulatory decisions.
- Complete 75 percent of projects identified in the Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) designed to lead to appropriate policy for applying modern *in vitro* and *ex vivo* technology to assess drug metabolism and drug interactions.
- Reduce the number per application of post-approval changes requiring chemistry supplements.
- Improve inspection coverage by inspecting 36 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers.
- Assure the FDA inspections of domestic drug manufacturing and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.

Rationale:

Research, postmarketing surveillance and international harmonization play an integral role in facilitating the availability of safe and effective drugs to the American consumer. The size of premarketing clinical trials means that FDA and the industry cannot learn everything about the safety of a drug before it is approved. Americans have chosen to accept this risk in order to have drugs developed within a reasonable time. The tradeoff is the continued vigilance of the Center and industry to collect and assess data during the postmarketing life of a drug.

The International Conference on Harmonization (ICH) brings together the regulatory authorities of Europe, Japan and the United States, and experts from the pharmaceutical industry to discuss scientific and technical aspects of product registration. The ICH process results in documents that recommend ways to find consistency in the implementation and application of technical guidance documents and requirements for product registration. The fourth biennial meeting of the ICH, held in Brussels, Belgium July 1997, demonstrated that work on more than three-quarters of the guidance documents has been completed. Because of this success the ICH steering committee

agreed to launch a second phase that will maintain the existing documents and develop a Common Technical Document.

Research advances the scientific basis for regulatory policy and ensures that policy and decisions are based on the best available science. Through the development of external collaborations with industry, academia, professional societies and other government laboratories, applied research has expanded significantly. After many years of coordination, FDA is in the final stages of creating the Product Quality Research Initiative (PQRI). FDA, the pharmaceutical industry, and academia will collaborate on research to support regulations and guidance documents for the types of product quality information that should be submitted to the Agency. This will enable consistent and reasonable requirements for all product quality information submitted, and will streamline the drug development and approval processes for industry and FDA.

Approaches, Skills, Technology and External Factors:

To facilitate international electronic communication, a working group was established to evaluate and recommend Electronic Standards for the Transfer of Regulatory Information that will meet the requirements of the pharmaceutical companies and regulatory authorities.

PQRI research programs will focus on research in various areas of product quality. Several approaches are being used to create PQRI. A Collaborative Research and Development Agreement is currently being developed to provide the formalizing mechanism for PQRI. The current proposed members of the collaboration include FDA, the American Association of Pharmaceutical Scientists, Pharmaceutical Research and Manufacturers of America, Generic Pharmaceutical Industry Association, National Association of Pharmaceutical Manufacturers, National Drug Manufacturers Association, National Pharmaceutical Alliance, and the Parenteral Drug Association. A PQRI steering committee has been established that will provide general direction to the initiative and oversight to the Technical Committees. Consideration for certain projects may occur competitively via a request for proposal process. A single academic site may be selected to be the central focus for initiative activities. Working groups will oversee and participate in all aspects of a research program.

The Center's Office of Testing and Research has developed the OTR Research Plan through a formal research planning process. The plan is updated annually and filed with the FDA Office of Science. Goals have been established in the following areas: clinical pharmacology, product quality, toxicology, and regulatory testing.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Develop a list of bulk drug substances that may be used in compounding and publish a rule to be used for pharmacy compounding.

Data Sources: Checklist for tasks required under FDAMA as approved by the Pharmacy Compounding Steering Committee

Baseline Data: Requirements of Section 127 of FDAMA

Goal Statement: Complete 25 percent of the research projects started in FY 1999 under the auspices of the Product Quality Research Initiative, a collaboration among FDA, industry and academia established to provide a scientific basis for policy and guidance development in the Center for Drug Evaluation and Research (CDER) on issues of drug product quality and performance.

Data Sources: Office of Testing and Research (OTR) Research Plan (dated November 24, 1997); "A Proposal - Product Quality Research Initiative (PQRI);" Memorandum of Agreement Between Food and Drug Administration and American Association of Pharmaceutical Scientists; and "Proposed Operating Principles for the Product Quality Research Initiative."

Baseline Data:

FY 1998:

Formalize the PQRI collaboration.

FY 1999:

Initiate research projects under direction of PQRI and continue to plan and review activities of Technical Committees and Working Groups.

Goal Statement: Complete 75 percent of research projects identified in the Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) designed to develop rational, scientific-based requirements for drug substances, drug products and excipients to ensure a high standard of drug product quality and product performance for making regulatory decisions.

Data Sources: Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) and Presentation, entitled "Division of Product Quality Research Program and Projects: Future Direction."

Baseline Data:

FY 1998:

Identify specific issues and areas of research focus and develop research protocols.

FY 1999:

Initiate research and apply appropriate technologies to address specific issues including, where necessary, establishing tests and models for accurate evaluation.

Goal Statement: Complete 75 percent of projects identified in the Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) designed to lead to

appropriate policy for applying modern *in vitro* and *ex vivo* technology to assess drug metabolism and drug interactions.

Data Sources: OTR Research Plan (dated November 24, 1997)

Baseline Data:

FY 1998:

Complete initial research and develop guidance for studies *in vitro*.

FY 1999:

Complete collaborative studies *in vivo* to confirm scale up from *in vitro* and to optimize metabolite: parent ratios.

Goal Statement: Reduce the number per application of post-approval changes requiring chemistry supplements.

Data Sources: Center-Wide Oracle Management Information System (COMIS) database with adjustments based on source document analysis.

Baseline Data:

FY 1998:

Formulate evaluation plan to establish baseline criteria. Analyze data on wide variability in the number of manufacturing supplements; determine if extraneous factors can be eliminated to establish a stable baseline. Establish what surrogate measures could be used in the absence of a stable baseline.

FY 1999:

Establish baseline against which a target level of reduced supplements can be set.

Goal Statement: Improve inspection coverage by inspecting 36 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers.

Data Sources: Program-Oriented Data System, Official Establishment Inventory

Baseline Data:

FY 1997:

26% of establishments inspected

FY 1998: 24%

FY 1999: 22%

Note about goal: This includes inspections done by FDA directly, or through state contracts or partnership agreements. Achievement of this goal relies on the willingness and ability of the states to contract with FDA to inspect a large portion of the medical gas repacker industry. To implement these contracts, FDA's experience predicts that a

significant investment in training and time is necessary to ensure quality and uniformity of inspections.

Note about Baseline Data: Fiscal year baseline data is an estimate derived from two-year coverage data. Two-year coverage is computed by dividing the number of establishments inspected in the last two years by the total number of registered establishments. The fiscal year baseline estimate is half this number.

Goal Statement: Assure the FDA inspections of domestic drug manufacturing and repackaging establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.

Data Source: FDA Field Data Systems

Baseline data:

FY 1997: 92%

FY 1998: 93%

FY 1999: at least 90% (target)

Note about goal: Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector.

Verification and Validation

Performance goals for the human drugs program were developed on the predication they could be measured to demonstrate goal achievement. Guidance that focused on how to develop outcome oriented, measurable, verifiable goals was provided to program/project managers at the beginning of the goal development process. Existing Agency systems such as COMIS (the Center-wide Oracle Management Information System), and the NDE (New Drug Evaluation System) will be used to collect, track and report on goals identified under application review.

COMIS is CDER's enterprise-wide system for supporting premarket and postmarket regulatory activities. It consists of multiple applications, or components, that store and retrieve data in a single integrated database. COMIS is the core database upon which most mission-critical applications are dependent. The NDE contains information about investigational new drug applications, NDAs, supplements, and amendments, and it tracks their status through the review process. Information includes status, type of

document, review assignments, status for all assigned reviewers, and other pertinent comments.

The Adverse Events Reporting System (AERS) continues to be developed and will be relied upon over ensuing years to provide accurate, accountable data for the performance goals identified in the strategic area of injury reporting. The goal of AERS is to support the strengthening of the Agency's postmarket surveillance program for all regulated products by providing a consistent, Agency-wide approach to the receipt and processing of adverse events information, to increase reporting of events by the health care community, and provide interactive two-way communication with the health care community and manufacturers. A schedule of program evaluations to be conducted over the next few years in major goal areas will be developed.

BIOLOGICS

Total Program Resources (FY 2000):	\$000	FTEs
Center	115,532	819
Field	22,582	248
Total	138,114	1,067

Program Overview

FDA is responsible for assuring that blood and blood products, blood test kits, bacterial vaccines and antigens, viral vaccines, therapeutic agents, and other biological products intended for use in the prevention, diagnosis, and treatment of diseases in humans are pure, potent, safe, and effective, as well as properly labeled for their intended uses.

The Biologics Program includes registration and inspection of blood banks and other firms processing blood; licensing and inspection of firms collecting human source plasma; evaluating and licensing biologics manufacturing firms and products; lot release of licensed products; removal of ineffective, unsafe, or improperly labeled products from the market; development of necessary regulations, compliance programs and guidelines; and conducting research, in concert with other DHHS public health agencies, academia, and industry, to further the development of new products and to provide a sound scientific basis for their regulation.

Program Strategic Goals

Strategic Goal 1:

Ensure the expeditious availability of safe and effective human drugs, including biologics, for the prevention, diagnosis, and treatment of disease.

Resources: \$30,685,000 187 FTEs

Performance Goals:

- Review and act on 90 percent of standard original New Drug Application (NDA), Product License Application (PLA) and Biologic License Application (BLA) submissions within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority original NDA/PLA/BLA submissions within 6 months of receipt.
- Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority efficacy supplements within 6 months of receipt.
- Review and act on 90 percent of manufacturing supplements within 6 months of receipt, and review and act on 50 percent within 4 months of receipt.
- Review and act on 90 percent of Class 1 resubmitted original applications within 4 months of receipt (review 50 percent within 2 months); and review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

Rationale:

The Food and Drug Administration Modernization Act of 1997 (FDAMA), Public Law 105-115, authorized revenues from fees paid by the pharmaceutical industry to expedite review by the FDA of human drug applications. These revenues were directed by section 101(4) of this Act toward accomplishment of goals identified in the letters of November 12, 1997 from the Secretary of Health and Human Services to the Chairman of the Energy and Commerce Committee of the House of Representatives, and the Chairman of the Labor and Human Resources Committee of the Senate.

The FDA's Center for Biologics Evaluation and Research (CBER) continued to improve the speed of its processes while completing 38 major approvals covering a broad spectrum of new products, technologies, manufacturing methods, indications and premarket applications in 1998.

In 1998, the greatest acceleration was seen in 20 approvals, involving 11 PLAs and BLAs and 9 PLA and BLA supplements, which were part of the prescription drug user fee program. The PLA/BLA user fee approvals were completed in the median time of 15.19 months, or 16 percent faster than the corresponding median time of 18.06 months in 1996. The median time for the approval of PLA/BLA supplements for user fee products last year was 11.94 months.

Achievement of the performance goals will expedite the availability of safe and effective biological products for the prevention and treatment of disease.

Approaches, Skills, Technology, External Factors:

Resources are primarily devoted to application review, but also include pre-submission meetings and pre-approval inspections.

The FDAMA authorizes the collection of user fees to enhance the review process of new human drug and biological products through FY 2002. The Act establishes fees for applications, establishments and approved products. The user fees have enabled the Agency to improve its performance for drug review and approval times. The median user-fee PLA approval time decreased from 22.5 months in FY 1994, to 15.2 months in FY 1998.

FDA has met or exceeded its Prescription Drug Use Fee Act (PDUFA) performance goals thus far. Meeting with sponsors early in the drug development process makes the process more efficient for industry and the Agency. Product license applications are of better quality and there are fewer refuse-to-file decisions.

FDA has initiated programs designed to make the application review process more efficient. One such initiative is the Managed Review Process. The Managed Review Process incorporates concepts of project management with the goal of producing high quality reviews in a timely manner. The system includes establishing specific time frames with interim milestones for the evaluation of both establishment and product license applications.

Factors that affect the Agency's ability to achieve the performance goals are: quality and complexity of applications; the number of applications received; commitments which take researchers/reviewers away from their assigned review work, such as regulation/guidance writing; and the Agency's ability to hire and train qualified researchers/reviewers as needed. Interaction between FDA scientific reviewers and scientific experts in industry enhances the reviewers' expertise in current product science and technology. CBER scientists use applied research programs to gain experience and establish standards for new therapies.

Performance Goals, Data Sources, and Baselines:

Note about Baseline Data: In several years the program performance (Baseline Data) exceeds the projected FY 2000 performance goals. The projected performance goals are as the Secretary committed to in her letters to Congress. "NA" means the goal is not applicable in that fiscal year.

Goal Statement: Review and act on 90 percent of standard original New Drug Application (NDA), Product License Application (PLA) and Biologic License Application (BLA) submissions within 12 months of receipt (50 percent within 10

months); and review and act on 90 percent of priority original NDA/PLA/BLA submissions within 6 months of receipt.

Data Sources: CBER's Biologics Regulatory Management System

Baseline Data:

Standard Applications within 12 months:

FY 1993: 86%

FY 1994: 100%

FY 1995: 100%

FY 1996: 100%

FY 1997: 100%

FY 1998: 90% (estimate)

FY 1999: 90% (target)

Standard Applications within 10 months:

FY 1997: NA

FY 1998: NA

FY 1999: 30% (target)

Priority Applications within 6 months:

FY 1997: 100%

FY 1998: 90% (estimate)

FY 1999: 90% (target)

Goal Statement: Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority efficacy supplements within 6 months of receipt.

Data Sources: CBER's Biologics Regulatory Management System

Baseline Data:

Standard Applications within 12 months:

FY 1993: 55%

FY 1994: 83%

FY 1995: 100%

FY 1996: 88%

FY 1997: 100%

FY 1998: 90% (estimate)

FY 1999: 90% (target)

Standard Applications within 10 months:

FY 1997: 44%

FY 1998: NA

FY 1999: 30% (target)

Priority Applications within 6 months:
FY 1997: 100%
FY 1998: 90% (estimate)
FY 1999: 90% (target)

Goal Statement: Review and act on 90 percent of manufacturing supplements within 6 months of receipt, and review and act on 50 percent within 4 months of receipt.

Data Sources: CBER's Biologics Regulatory Management System

Baseline Data:

Within 6 months:
FY 1993: 53%
FY 1994: 85%
FY 1995: 94%
FY 1996: 98%
FY 1997: 98%
FY 1998: 90% (estimate)
FY 1999: 90% (target)

Within 4 months:
FY 1997: 26%
FY 1998: NA
FY 1999: 30% (target)

Goal Statement: Review and act on 90 percent of Class 1 resubmitted original applications within 4 months of receipt (review 50 percent within 2 months); and review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.

Data Sources: CBER's Biologics Regulatory Management System

Baseline Data:

The breakdown of resubmitted original applications into classes 1 and 2 is a new definition prescribed in the FDAMA beginning in 1998. FDA has not tracked the applications using the new definitions in the past. Data showing the percentage reviewed within prescribed time frames during FY 1998 will not be available until mid-FY 1999.

Resubmissions within 6 months:
FY 1998: 90% (estimate)

Class 1 resubmissions within 6 months:
FY 1998: 90% (estimate)
FY 1999: NA

Class I resubmissions within 2 months:
FY 1998: 30% (estimate)
FY 1999: 50% (target)

Class I resubmissions within 4 months:
FY 1998: NA
FY 1999: 90% (target)

Class II resubmissions within 6 months:
FY 1998: NA
FY 1999: 90% (target)

Strategic Goal 2:

Ensure the safety and effectiveness of non-user-fee biological products such as blood and blood products, biotechnology-derived hematologics, allergenic products, and devices associated with their manufacture.

Resources: \$72,286,000 542 FTEs

Performance Goal:

- Review and act on 85 percent of complete blood bank and source plasma Product License Application (PLA)/Biologic License Application (BLA) submissions, and 90 percent of PLA/BLA Major supplements within 12 months after submission date.

Rationale:

The mission of the Blood Program is to ensure that blood, blood products, biotechnology-derived hematologics, and devices associated with their manufacture and use are safe, effective, and adequately labeled.

The blood supply is critical to the nation's health care system, and the United States has the safest blood supply in the world. Each year approximately 14 million blood units are drawn from volunteer donors for use in more than 3.5 million Americans. FDA vigorously continues to strengthen its efforts to protect the nation's blood supply, and to minimize any risk to patients acquiring the human immunodeficiency virus (HIV), hepatitis, Creutzfeldt-Jakob disease (CJD), and other bloodborne diseases.

Achievement of the performance goals will facilitate the availability of safe and effective source plasma and blood bank products for the treatment of disease and injury.

Approaches, Skills, Technology, and External Factors:

FDA reviews and evaluates premarketing license applications for blood establishments and blood products. The Agency also conducts research of blood and blood products pertinent to its regulatory mission. FDA will continue to develop regulations to screen and test donors for infectious diseases. FDA will also extend its current blood oversight, and regulation revitalization and reinvention project. The major areas to be addressed include: development of the BLA as it applies to blood establishments; development of Agency-wide goals and direction; coordination of Agency-wide resources to protect the blood supply; and the revitalization and rewrite of blood regulations.

With FDAMA, resources need to be expended in the early product development stages for consultation. Additional resources are required to have meaningful dialogue between the sponsor and the appropriate FDA staff during early stages and to also perform the on-going application reviews. Otherwise, application review times will slip or the appropriate expertise will not be available for the sponsor meetings and commitments will be made to do studies that are not in the best interest of the public health. In addition, enforcement/compliance actions appear to be increasing. These also detract from application review resources.

Factors which affect the Agency's ability to achieve the performance goals are: the quality and complexity of applications, the number of applications received, and commitments which take researchers/reviewers away from their assigned review work, such as regulation/guidance writing.

The ability of FDA to protect the nation's blood supply is enhanced through scientific efforts to understand HIV, hepatitis, CJD, and other bloodborne diseases. The ability of CBER scientific reviewers to ensure the safety and efficacy of blood screening tests and other new technology is increased through applied regulatory research.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Review and act on 85 percent of complete blood bank and source plasma Product License Application (PLA)/Biologic License Application (BLA) submissions, and 90 percent of PLA/BLA Major supplements within 12 months after submission date.

Data Sources: CBER's Biologics Regulatory Management System

Baseline Data:

Complete Submissions:

FY 1993: 34%

FY 1994: 43%

FY 1995: 84%

FY 1996: 95%

FY 1997: 83%

FY 1998: 70% (estimate)

FY 1999: 60% (target)

Major Supplements:

FY 1997: 98%

FY 1998: 90% (estimate)

FY 1999: 90% (target)

Strategic Goal 3:

Inform and assist biologics manufacturing firms to achieve compliance with Good Manufacturing Practices (GMPs) and manufacturing regulations.

Resources: \$ 35,143,000 338 FTEs

Performance Goals:

- Assure that FDA inspections of domestic biologics manufacturers and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high conformance rate (at least 90 percent) with FDA requirements.
- Increase the percentage of plasma fractionator establishments in compliance with Current Good Manufacturing Practices (CGMPs) to 80 percent.
- Meet the biennial inspection statutory requirement by inspecting 50 percent of registered blood banks, source plasma operations, and biologics manufacturing establishments.

Rationale:

FDA is required by law to conduct biennial inspections of all licensed establishments to determine compliance with Current Good Manufacturing Practice (CGMP) regulations and to ensure compliance with applicable product and establishment standards and license commitments. In addition, FDA inspects all manufacturing facilities, which are unlicensed and/or under contract to a licensed establishment. FDA conducts biomedical research inspections to review pivotal clinical trial data, and in inspections of new tissue-cellular-based products.

"Team Biologics," a plan to revamp FDA inspections of biologics facilities by relying on investigator teams led by the Office of Regulatory Affairs (ORA), began implementation in late FY 1997. By transferring the lead responsibility for biologics postmarket inspections from CBER to ORA, all FDA CGMP inspections will be standardized by having a single Agency unit conduct inspections using a consistent approach. A core team of inspectors lead the inspections. The inspectors receive special training in performing inspections of biologics facilities, such as blood banks and plasma establishments. CBER product experts are also part of Team Biologics. They will be key in providing advice to their field colleagues on the team. This allows CBER/ORA to focus specially trained field investigators on the activities under this high priority program.

By accomplishing the performance goals the Biologics Program will ensure that biologics establishments are in compliance with regulations and that the products produced in those establishments are pure.

Approaches, Skills, Technology, and External Factors:

In addition to enhancing quality assurance procedures in blood banks, FDA will be defining new strategies for blood bank inspections based on control processes for critical production points. The Agency will also provide training programs for inspectors to implement the new approaches; conduct workshops to clarify Agency expectations for industry; and evaluate the need for changes in the error and accident reporting requirements.

FDA will continue to improve donor-eligibility criteria and deferral programs. It will also continue studies to assess the effectiveness of donor interview and education programs, and coordinate a national effort to address concerns regarding donor-deferral registries.

FDA will continue to collaborate closely with other government and non-government regulatory organizations such as the National Institutes of Health, Centers for Disease Control and Prevention, state health agencies, the American Red Cross, and the American Association of Blood Banks to assure that all policies are mutually consistent in guarding the safety of the nation's blood supply.

Factors which affect the Agency's ability to achieve the performance goals are unanticipated crises such as product tampering, which require immediate investigative and enforcement actions and take inspectors/investigators away from their planned assignments.

The availability of qualified scientific personnel to review, evaluate and investigate postmarket adverse events affects the Agency's ability to make sound and timely decisions concerning recalls and withdrawals.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Assure that FDA inspections of domestic biologics manufacturers and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high conformance rate with FDA requirements (at least 90 percent).

Data Sources: FDA Field Data Systems

Baseline data:

FY 1997: 92%

FY 1998: 97%

FY 1999: at least 90% (target)

Note about Goal: Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector.

Goal Statement: Increase the percentage of plasma fractionator establishments in compliance with Current Good Manufacturing Practices (CGMPs) to 80 percent.

Data Sources: Field Accomplishment and Compliance Tracking System (FACTS)

Baseline Data:

There are 26 foreign and domestic plasma fractionator establishments.

FY 1996:

12 establishments were inspected and 9 were in compliance (75%)

FY 1997:

The Agency performed 25 inspections of 23 plasma fractionator establishments. One of the establishments was found not to be in production. Of the remaining 22 establishments, 9 were classified as being essentially in compliance (41%)

FY 1998:

13 of 24 plasma fractionator establishments were considered in compliance (54%)

FY 1999:

Compliance rate of 70% (target)

Goal Statement: Meet the biennial inspection statutory requirement by inspecting 50 percent of registered blood banks, source plasma operations and biologics manufacturing establishments.

Data Sources: Program-Oriented Data System, Official Establishment Inventory

Baseline Data:

FY 1997: 46% of establishments inspected

FY 1998: 46%

FY 1999: 43% (target)

Note about Goal: This includes inspections done by FDA directly, or through state contracts or partnership agreements.

Note about Baseline Data: Fiscal year baseline data is an estimate derived from two-year coverage data. Two-year coverage is computed by dividing the number of establishments inspected in the last two years by the total number of registered establishments. The fiscal year baseline estimate is half this number.

Verification and Validation

The Biologics Program uses various databases to manage its diverse programs and to assess performance. The principal CBER database is the Biologics Regulatory Management System (BRMS). The BRMS is CBER's VAX-based, Oracle database that is used to track all PLA, BLA, and supplement submissions; provide information to facilitate the review process (product, application status, milestone tracking, facility, review committee, industry contacts, and other information); and produce a wide variety of management reports. The BRMS records application review information on each license application and supplement received and filed by the Center. The BRMS records information about PDUFA and non-PDUFA license applications. The milestone tracking module is used to track and report on CBER's PDUFA goals. Data entry is done in each of the offices' application review divisions. The Regulatory Information Management Staff (RIMS) monitors and is responsible for maintaining data quality and integrity in BRMS.

The Biologics Investigational New Drug (IND) Management System (BIMS) is CBER's VAX-based, Oracle database that is used to track all Investigational New Drug Applications (IND), Investigational Device Exemption (IDE), and Master Files (MF) submissions (nearly 11,000 in 1997); provide product, application status, and other information to facilitate the review process; and produce a wide variety of management reports. The system also stores summaries of telephone conversations and meetings related to the submissions, as well as actually generating some of the correspondence to sponsors. Most data entry is done by the Document Control Center (DCC) or the Consumer Safety Officers in each office's application review division. There are numerous mechanisms established for quality control in DCC, the application review offices, the Regulatory Information Management Staff, and several built into BIMS itself.

The Blood Logging and Tracking System (BLT) is under development by the Office of Blood Research and Review (OBRR) to record and track the various applications reviewed by that Office. The OBRR receives and reviews a wide variety of application types. PLAs, ELAs (Establishment License Applications) and BLAs are tracked by the BRMS, discussed above. INDs are tracked by the BIMS, also discussed above. The Office utilizes the BLT to record and track data concerning new drug applications (NDAs) and NDA supplements, device premarket applications (PMAs) and PMA supplements, 510(k)s, and Abbreviated New Drug Application (ANDAs) and ANDA supplements.

The data retrieved from these systems are reviewed and validated by the RIMS and the application review offices. If errors are detected the errors are corrected.

Federal regulations (21 CFR, Part 600.14) require reporting of errors and accidents in the manufacture of biological products that affect the safety, purity, or potency of the product. The error and accident reporting process enables the Agency to evaluate and monitor establishments, to provide field staff and establishments with trend analyses of the reported error and accident types, and to respond appropriately to reported errors and

accidents to protect the public health. The regulation applies only to licensed manufacturers.

In May 1995, the DHHS Office of the Inspector General issued a report recommending that the reporting requirements be expanded to include unlicensed blood banks and transfusion services. A proposed rule was issued on September 23, 1997, that expands the reporting requirement to all biological product manufacturers regulated by FDA.

In the past five years, the Agency has received an average of 12,000 error and accident reports annually. FDA estimates that over 116,000 error and accident reports would be received under the proposed regulation. FDA does not have a computer system to permit the electronic submission of error and accident reports. If the Agency is to comply with the intended goals of the error and accident reporting regulation, it will need a system that would allow it to receive electronic submission of reports; and to review, process, and analyze more than 100,000 reports annually.

The Biologics Program relies on the Office of Regulatory Affairs' Field Accomplishments and Tracking System (FACTS) to register and record biologics manufacturing establishment inspection and compliance data. FACTS versions 1 and 2 together will replace the several dozen applications that comprise the current Field Information System. The software development contractor delivered FACTS version 1 to the FDA on September 30, 1997. Version 1 functionality includes all sample collections; all sample tracking, accountability, and dispositions; sample analysis of pesticides, additives, colors, elements, mycotoxins and radionuclides; firms inventory, maintenance and registration; work assignments and work management; and other features.

Meanwhile, the design and development of FACTS version 2 is underway. Major features of version 2 include replacing the remaining FIS functions: remainder of lab analyses; rest of investigations including records and tracking; compliance functions; other core items including personnel management (MUS); and miscellaneous operations including recalls and audit checks. The delivery to FDA of version 2 is scheduled for October 31, 1998, to be followed by the same implementation scenario as is being used for version 1.

ANIMAL DRUGS AND FEEDS

Total Program Resources (FY 2000):	\$000	FTEs
Center	36,375	293
Field	16,098	176
Total	52,473	469

Program Overview

The Center for Veterinary Medicine is responsible for increasing the availability and diversity of safe and effective veterinary products that relieve pain and suffering, sustain health, improve animal productivity, and do not compromise public health. The primary goals are to: 1) ensure that only safe and effective animal drugs, devices, feeds and feed additives are marketed; 2) ensure that foods from animals that are administered drugs and food additives, in accordance with label directions, are safe for human consumption; and 3) to work proactively to increase the availability and diversity of safe and effective products for use by the agricultural community.

The Agency strives to process New Animal Drug Applications (NADAs) as quickly as possible to ensure that only safe and beneficial veterinary drugs, intended for the treatment and/or prevention of diseases in animals, and the improved production of food producing animals, are approved for use. In addition, FDA maintains continuing surveillance over all animal drugs, devices, and feeds marketed in interstate commerce in order to minimize threats to human and/or animal health which might arise as a result of the use of these products.

Surveillance of marketed products and the regulated industry is accomplished through review of drug experience reports and by the FDA field offices through inspections, sample collections and analysis, investigations, and other postmarket activities. Regulatory actions are taken as needed to control violative goods and firms.

Methodology development and validation as well as collaborative studies are accomplished through in-house research at the Center for Veterinary Medicine Research Office in Laurel, Maryland, the Veterinary Research Center in Denver, Colorado, and via special projects in FDA's other laboratories. Collaboration with other agencies such as the Centers for Disease Control and Prevention (CDC) and the U.S. Department of Agriculture (USDA) is accomplished through interagency agreements. FDA also funds extramural research via contract and cooperative agreements and through collaboration with the University of Maryland known as the Joint Institute for Food Safety and Applied Nutrition (JIFSAN).

Program Strategic Goals

Strategic Goal 1:
Increase the availability and diversity of safe and effective animal products.

Resources: \$17,515,350 207 FTEs

Performance Goals:

- Update 10 percent of the animal drug review guidelines which serve as aids to industry in the animal drug review process.

- Review and act on 65 percent of New Animal Drug Applications (NADAs)/Abbreviated New Animal Drug Applications (ANADAs) within 180 days of receipt.
- Maintain a 75 percent level for pre-submission conferences with industry sponsors.
- Reduce drug development and review time through implementation of additional phases of electronic submission in the investigational new animal drug development process.
- Increase bioresearch monitoring inspections completed and results received to 115.

Rationale:

The availability of safe and effective drugs allows food animal producers to maintain healthy animals with assurance that products will be safe, wholesome, and free of drug residue when they reach the consumer. Over time, animal drug use moved from therapeutic treatment to save individuals or herds of animals intended for human consumption to the routine use of production drugs, which helps the producer maintain a profit margin while keeping safe and wholesome animal products at a reasonable cost for the average American consumer. Today's approval process not only addresses the effectiveness of drugs or chemicals, but also determines withdrawal times, which ensure that the animal product is residue-free when offered for purchase to the consumer.

In addition, the approval process includes bioresearch monitoring. Bioresearch monitoring is an integral part of the pre-market application review process. Inspections assure that sponsors are in compliance with regulations and good laboratory practices are followed. Bioresearch monitoring inspections provide a mechanism to alert the Agency to potential problems. FDA works with the industry to ensure that they are actually capable of producing the product under review and that the data supporting the review is valid.

Availability of safe and effective drugs affects the health and well-being of companion as well as food producing animals and provides the U.S. citizen with an economical and safe food supply. In addition to the economic impact on the agricultural community, an immediate outcome is increased availability of drugs to treat companion animals, thereby increasing their life span and the quality of life. Studies have shown that companion animals have a positive effect on the quality of life of selected segments of the human population. Companion animals are used to increase independence of individuals with disabilities such as guide dogs for the blind, working dogs for the deaf, and a variety of animals that assist physically challenged individuals. The elder population and individuals in institutions also appear to benefit from associations with companion animals, according to recent studies.

In order to increase the availability and diversity of safe and effective products, the Animal Drugs and Feeds Program will expedite and facilitate the approval of new animal drugs by implementing the Animal Drug Availability Act⁽¹⁾ of 1996 (ADAA), the FDA Modernization Act (FDAMA)⁽²⁾ and our reinventing government (REGO) initiative. The

Animal Drugs and Feeds Program will inform and assist product sponsors throughout the approval process starting with the pre-submission conference. The focus will be on informing and assisting firms in complying with the new legislation and streamlining the product review process by continuing the implementation of the phased review process. Streamlining efforts will be focused on reducing the overall time required for drug development from product conception by the drug sponsor through the Investigational New Animal Drug phase to the new animal drug approval. FDA has initiated processes to obtain input from our stakeholders in order to develop meaningful performance measures to assess progress consistent with our reinvention initiatives. Better automated information systems, including those supporting electronic submission of applications by sponsors, are being developed to facilitate and expedite the review process. CVM successfully completed a pilot project to permit one type of electronic submissions for review and plans to expand the submission program to include other regulatory reporting requirements.

The immediate outcome from these performance goals will be a decrease in the developmental time and costs associated with research studies and other drug approval regulatory requirements. Pre-submission conferences and availability of CVM guidelines through the Internet and workshops will help increase industry efficiency, thereby reducing overall developmental costs. There will be more industry collaboration and partnerships to expedite the process. Phased review will provide more timely feedback and provide "early detection" of application deficiencies.

Another immediate outcome is an overall shortened review time. The change in processes is designed to decrease overall review time thereby increasing the availability of safe and effective animal drugs. Phased review coupled with improved information systems such as electronic submission of applications and enhancements to the Submission Tracking and Review System (STARS) will allow FDA to more efficiently perform review activities. This will enable the agricultural community to more effectively provide animal derived products, possibly at a lower cost due to the reduced animal drug developmental costs being reflected in lower costs to purchasers.

A primary ultimate outcome is safe animal products for human consumption. Veterinarians and the agricultural community need animal drugs to ensure a safe food supply. As disease-causing agents mutate and become resistant to current drugs, new drugs are needed.

Approaches, Skills, Technology, and External Factors:

Resources are primarily devoted to new animal drug review, but also include surveillance activities in the field, as well as research that supports the review process.

A sponsor notifies CVM about the development of a new animal drug. CVM works with the sponsor to set up a pre-submission conference. The conference can be conducted in person or by audio or video teleconference. Information exchange continues throughout the research and development process. As the sponsor completes a technical section (the

different pieces of a New Animal Drug Application), it is submitted to CVM for review. The technical sections include target animal safety and effectiveness, manufacturing methods and control chemistry, residue chemistry and regulatory methods, human food safety, and environmental safety.

Guidance documents are available to industry to facilitate the accurate and complete preparation of drug applications. Development of new guidance documents and updating existing documents to reflect recent changes in legislation will be initiated in FY 1999 and continued in FY 2000. Dependent on workload and reviewer expertise guidance documents will be reviewed and updated.

In addition to teleconferences, FDA uses the Internet technology to support electronic submission of data and to post guidance documents for stakeholders' access.

The results of routine postmarket surveillance activities and special surveys conducted to assure that sponsors are in compliance with regulations are used in the pre-approval process to ensure data integrity and Good Manufacturing Practices. Pre-approval inspections are also conducted as needed to enhance understanding and confirm that the sponsor has the ability to produce a safe and effective product.

Research is an essential element in the approval process. Method validation studies are necessary in approving applications for new drugs for food animals.

Information system development improves the ability of primary reviewers to access Agency and sponsor data used in the review process.

New animal drug review activities are supported by scientific research, data collection, and analysis. Review activities are conducted primarily by staff in CVM's Office of New Animal Drug Evaluation with support from other parts of the Center. Scientists provide guidance and assistance to industry, consumers, and other constituencies regarding regulatory interpretations related to animal drugs and feeds. They also serve as national experts by providing technical expertise for the development and harmonization of international specifications and standards in the area of veterinary medicine.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Update 10 percent of the animal drug review guidelines which serve as aids to industry in the animal drug review process.

Data Sources: CVM's priority project tracking system.

Baseline Data:

FY 1998:

Review guidance documents to identify documents for preparation or rewriting.

FY 1999: 1% (target)

Goal Statement: Review and act on 65 percent of New Animal Drug Applications (NADAs)/Abbreviated New Animal Drug Applications (ANADAs) within 180 days of receipt.

Data Sources: Submission Tracking and Review System (STARS)

Baseline Data:

FY 1997: 75%

FY 1998: 75%

FY 1999: 65 % (target)

Goal Statement: Maintain a 75 percent level for pre-submission conferences with industry sponsors.

Data Sources: Submission Tracking and Review System (STARS)

Baseline Data:

FY 1997: 75%

FY 1998: 75%

FY 1999: 75% (target)

Goal Statement: Reduce drug development and review time through implementation of additional phases of electronic submission in the investigational new animal drug development process.

Data Sources: CVM's priority project tracking system.

Baseline Data:

FY 1997:

Initiated the development of infrastructure/procedures

FY 1998:

Completed pilot to permit electronic submissions of Notices of Claimed Investigational Exemptions (NCIE)

FY 1999:

2 phases (target):

Drug Shipment Notices

Notices of Slaughter

Goal Statement: Increase bioresearch monitoring inspections completed and results received to 115.

Data Sources: CVM Bimo Tracking Database

Baseline Data:

FY 1997: 57 inspections

FY 1998: 46

FY 1999: 50 (target)

Strategic Goal 2:

Minimize the threat to humans and/or animal health that might arise as a result of the misuse or illegal use of animal drugs, devices, and feeds marketed in interstate commerce.

Resources: \$27,257,650 232 FTEs

Performance Goals:

- Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high level of conformance (at least 90 percent) with FDA requirements.
- Meet the statutory biennial inspection requirement by inspecting 50 percent of registered animal drug and feed establishments.
- Maintain the number of Adverse Drug Event (ADE) reports reviewed at 7,000 through consumer participation in the pharmacovigilance program for veterinary drugs by publication and distribution of educational material.
- Improve our ability to monitor for Adverse Events by initiating the development of an integrated agency-wide system.

Rationale:

Surveillance of marketed products and the business industry is accomplished through review of drug experience reports and compliance programs implemented by the FDA field offices through inspections, sample collections and analysis, investigations, and other activities. Regulatory actions are taken as needed to control violative goods and firms.

FDA has a statutory obligation to inspect all regulated animal drug and feed establishments once every two years. Currently we are inspecting these establishments once every four years. At the same time there has been an increased emphasis on postmarket monitoring as a result of public demand for increased drug availability. With limited resources, routine inspections have lower priority than inspection of firms producing high profile products. This has an impact on the pre-approval process which requires a "recent" inspection prior to approval of a new animal drug.

Drug Experience Reports, including Adverse Drug Event (ADE) data on adverse drug reactions, are important in the monitoring for reactions that were not found in the preapproval research trials. The immediate outcome of our surveillance systems is the identification of potential human and/or animal health hazards. A group of similar reports submitted in a short period of time may alert CVM and the drug company to a problem with a particular lot of drug. This may result in a product recall of that affected lot. We

plan to integrate our database with an Agency database to better monitor the interaction of products and provide baseline data on the rate and characteristics of injuries. Another intermediate outcome would be for a label change to include new information gleaned from reported ADEs. An intermediate outcome is the development of procedures and strategies to prevent, minimize, or contain problems such as informing the veterinary community of adverse reactions due to drug interactions that were not apparent in clinical trials or withdrawal of marketed drugs as necessary to protect human and animal health. Veterinarians in practice depend on the information available in drug labeling to make informed choices about the risks and benefits associated with the use of a drug. The ultimate outcome is assurance that marketed animal drugs and food additives provide for safe food products derived from animals and ensure quality health care of animals.

In addition to information on the label, veterinarians and other health care professionals are influenced by the promotion and advertising activities of the industry. FDA protects practitioners and the general public by reviewing such material for false and misleading promotions. Inaccurate or false information can lead to a compromise of therapy which can result in injury or death. The immediate advertising and promotion review outcome is a decrease in fraudulent and misleading information which promotes off-label use. The ultimate outcome is a reduction in the use of ineffective treatments and associated economic fraud.

The CVM drug listing database, in conjunction with ADE data is a powerful tool that allows CVM to properly serve the veterinary and animal health community, by providing information on approved and unapproved products, and veterinary drug shortages. This information enables proper surveillance and monitoring of the animal drug and feed industry, and therefore gives CVM the ability to act proactively to avert crises before they happen.

CVM is improving outreach efforts in the area of consumer education and feedback by using state-of-the-art communication technologies including publicizing information in a dedicated section of the CVM home page that incorporates issues of consumer interest and provides a mechanism for consumer comment. CVM is also making a strong effort to educate its partners in industry by publishing and disseminating guidance, training initiatives in targeted high-risk compliance areas, and in working more closely with industry to resolve problems.

Approaches, Skills, Technology, and External Factors:

Resources are primarily devoted to monitoring and surveillance activities including FDA Field inspections/investigations, data review and analysis, educational initiatives, scientific research, and development of compliance and enforcement strategies.

FDA will reduce the availability of unsafe animal drugs through improving/enhancing our compliance strategy. Through development of partnership relationships with industry and the states, we will implement the ADAA through new regulations, implement the

FDAMA requirements, and develop educational initiatives. As needed, we will develop enforcement strategies to assure public safety.

CVM is notified about potential postmarket problems via one or more of our early warning systems. Center employees review National Antimicrobial Resistance Monitoring System (NARMS) data, ADE reports, Establishment Inspection Reports (EIRs), Contamination Response System (CRS) data, Tissue Residue Information System (TRIMS), Residue Violation Information System (RVIS), or other forms of communication. FDA then takes the appropriate action to address emerging issues, prevent or contain problems, and bring the animal drug industry into compliance.

Routine postmarket surveillance activities and special surveys are conducted to assure that sponsors are in compliance with regulations designated to ensure data integrity and Good Manufacturing Practices. CVM partners with other federal and state agencies, our stakeholders, and regulated industry to develop and sponsor workshops, symposia, and publications with a focus on prevention in order to assure the public that accurate information is disseminated and that marketed animal drugs and feeds are safe and effective.

Experience has shown that educational and partnership efforts are a good investment. Education and increased cooperation between FDA and regulated industry does decrease the need for enforcement actions and litigation. Recent decreases in our base budget have resulted in decreased training and other educational efforts. An increase in our base is needed to offset this trend.

Research is an essential element in postmarket assurance. Research studies are necessary in order to develop methods for detecting drugs, chemicals, pesticides, heavy metals, and microbial contaminants and residues that are potential health hazards.

Compliance and enforcement strategies are necessary in order to ensure animal and human health. Consumer Safety Officers utilize scientific and legal knowledge to develop and support strategies that encourage voluntary compliance and take enforcement action when necessary. Knowledge of food and drug law supports compliance activities and facilitates communications with FDA's Office of the Chief Counsel and the Department of Justice.

Program and systems analysts provide services and develop information systems focused on improving the ability of data exchange within the Agency and external to the Agency. Communication with the scientific community is an essential element in ensuring that FDA continues to make valid scientifically-based decisions.

Postmarket assurance activities are supported by scientific research, data collection, and analysis. Surveillance and compliance activities are conducted primarily by staff in CVM's Office of Surveillance and Compliance. Scientists, analysts, and Consumer Safety Officers in other parts of the Center such as the Office of Research and the Office of Management and Communications also support the postmarket assurance activities.

Scientists provide guidance and assistance to industry, consumers, and other constituencies regarding regulatory interpretations related to the marketing and use of approved animal drugs and feeds. Consumer Safety Officers work with animal scientists, veterinarians, and the Office of Chief Counsel to ensure both human and animal health.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high level of conformance (at least 90 percent) with FDA requirements.

Data Sources: FDA Field Data Systems

Baseline data:

FY 1997: 95%

FY 1998: 95%

FY 1999: at least 90% (target)

Note about goal: Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector.

Goal Statement: Meet the statutory biennial inspection requirement by inspecting 50 percent of registered animal drug and feed establishments.

Data Source: Program-Oriented Data System, Official Establishment Inventory

Baseline Data:

FY 1997: 31% of establishments inspected

FY 1998: 34%

FY 1999: 27% (target)

Note about Goal: This includes inspections done by FDA directly, or through state contracts or partnership agreements on manufacturers, repackers and relabelers (drugs), and manufacturers and growers requiring a Medicated Feed Mill License.

Note about Baseline Data: Fiscal year baseline data is an estimate derived from two-year coverage data. Two-year coverage is computed by dividing the number of establishments inspected in the last two years by the total number of registered establishments. The fiscal year baseline estimate is half this number.

Goal Statement: Maintain the number of Adverse Drug Event (ADE) reports reviewed at 7,000 through consumer participation in the pharmacovigilance program for veterinary drugs by publication and distribution of educational material.

Data Sources: Adverse Event Reporting System.

Baseline Data:

FY 1996: 3345 ADE reports.

FY 1997: 4134 ADE reports

FY 1998: 8000 ADE reports

FY 1999: 7000 ADE reports (target)

Goal Statement: Improve our ability to monitor for Adverse Events by initiating the development of an integrated agency-wide system.

Data Sources: CDER/CVM Injury Reporting Database

Baseline Data:

FY 1998: Identified gaps in data

FY 1999: Determine data base/systems to be integrated

Strategic Goal 3:

Further reduce the incidence of foodborne illness by monitoring for antimicrobial resistance, developing strategies to address antimicrobial resistance problems, improving current surveillance capabilities, continuing related research studies, and increasing awareness through educational initiatives.

Resources: \$7,700,000 30 FTEs

Performance Goals:

- Maintain the bacterial isolate testing rate from human and animal origin in the National Antimicrobial Resistance Monitoring System (NARMS) database at 2,000 and 4,000 respectively.
- Properly target resources related to education and enforcement initiatives by maintaining the number of follow-up violative tissue residues investigations at 600 in targeted food-producing animals.
- Increase the scientific basis for prioritizing research and surveillance activities by increasing the number of risk assessments performed regarding antimicrobial products to two per year.
- Expand the geographical scope and capacity of the National Antimicrobial Resistance Monitoring System (NARMS) by the establishment of an international resistance database.

Rationale:

Foodborne disease is a serious and growing problem in the United States. There are an estimated 6.5 to 33 million foodborne illnesses in the United States per year. There are approximately 9,000 deaths per year. The estimated hospital costs are \$3 billion per year.⁽³⁾ The U.S. population needs an effective early-warning system that can detect outbreaks early and allow implementation of intervention strategies to prevent their spread. Such a system will also advance understanding of foodborne illness and further prevention efforts.

A major part of the surveillance aspect of the CVM's Food Safety Initiative (FSI) is the National Antimicrobial Resistance Monitoring System (NARMS) which was initiated in 1996. This collaboration among FDA, CDC, and USDA to monitor bacterial foodborne pathogens for changes in antimicrobial susceptibility has greatly improved our ability to detect emerging resistance among foodborne pathogens and thereby help ensure the continued effectiveness of both human and veterinary drugs and aid in increasing the availability and distribution of effective drugs.

The initial effort in the development of an early warning system enabled the federal partners to identify the presence of a multi-drug resistant *Salmonella typhimurium* DT 104 (StmDT104) in humans and animals in the United States. This early warning of a potential epidemic, such as that seen in the United Kingdom, enabled CDC to warn state health departments of StmDT104's presence and to allow augmented monitoring for this pathogen. As a result, public health officials were prepared for the outbreak in Vermont and were in a position to take preventative steps to minimize the spread.

The impact of improving risk assessments will be to focus public resources on reducing those risks that have the greatest consequences for human health. Risk assessment provides a strong foundation upon which efficient allocation of scarce food safety resources can be made. Furthermore, risk assessment often plays a central role in the development of any science-based system of preventative controls.

Food safety research is critical to developing the means to more rapidly and accurately identify and characterize foodborne hazards to provide the tools for regulatory enforcement and to develop effective interventions that can be used, as appropriate, to prevent hazards at each step from production to consumption.

An integral part of the overall food-safety initiative is providing food safety education to a variety of audiences: consumers (the general public and specific groups at risk for foodborne illness); veterinarians, animal and other food producers. The challenge is to create effective education messages that address the risks relevant to each audience throughout the food chain.

The immediate outcome is an increase in our ability to detect new foodborne challenges and to intervene where possible to prevent or minimize disease outbreaks. The intermediate outcome is the development of strategies to address potential human and

animal health hazards. The ultimate outcome is a decrease in foodborne illnesses among both humans and animals.

Approaches, Skills, Technology, and External Factors:

In order to assure that foods from animals are safe for human consumption, FDA works with other government agencies, state and local governments, and the private sector to take action to prevent or minimize potential public health hazards through development of early warning systems, postmarket inspections and investigations, risk assessment, scientific research, educational initiatives and regulatory action.

Research is an essential element in postmarket assurance. Research studies are necessary in order to develop methods for detecting drugs and drug residues that may be present in food products derived from animals. In addition to methods development, analytical methods development research improves the effectiveness of monitoring for antibiotic resistance patterns as well as providing more rapid and accurate procedures to detect and quantify chemical substances in foods.

The NARMS was initially developed by expanding or redirecting existing programs in several federal agencies. The system is a collaborative effort of FDA, CDC, and USDA. The NARMS is the basis for regulatory decision making, food animal drug policy and identification of disease trends in human and animal medicine. It allows the detection of potential health hazards through systematic collection, analysis and interpretation of antimicrobial susceptibility surveillance data. In addition, the program serves as a basis for educational efforts and prudent drug use campaigns in humans and in veterinary medicine.

FDA and USDA work together to develop USDA's annual residue prevention sampling plan. The USDA Food Safety Inspection Service (FSIS) implements the plan using HACCP (critical control points) principles. If the sampling plan reveals a residue violation, FDA is notified via the USDA/FDA Residue Violation Information System (RVIS). FDA partners with the states to perform follow-up investigations. If this is a first time violation, through contracts and informal agreements, FDA trained state inspectors determine the "cause" of the violation and provide the educational information in order to prevent future violations. Feedback from the investigations is input into the Tissue Residue Information Management Systems (TRIMS). TRIMS data is used to identify trends and provide a basis for the development of additional educational material.

Increased activities in education in FY 1999 FSI include supporting government agencies and veterinary trade associations in the dissemination of antimicrobial "Judicious Use" or "Prudent Use" principles concerning treatment of food animals. In addition, conducting town hall meetings, symposia and inter-active teleconference with food animal veterinarians and producers in the U.S. and its trading partners so that all have a hand in developing a U.S. program that acknowledges the international guidelines.

A major portion of the educational increases will be done in partnership with state and local governments. FDA will work directly with state and local authorities who will facilitate the distribution of prudent and judicious drug use materials and programs developed by FDA. Other programs will be developed in conjunction with our state and local government agency counterparts. We will also partner with veterinary practitioners and producer groups as well as academia (veterinary medical schools) to increase awareness related to proper use of veterinary drugs.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Maintain the bacterial isolate testing rate from human and animal origin in the National Antimicrobial Resistance Monitoring System (NARMS) database at 2,000 and 4,000 respectively.

Data Sources: FDA-CDC-USDA National Antimicrobial Monitoring Program

Baseline Data:

Calendar Year 1996:

Salmonella Isolates: 1272 Human, 1921 Veterinary

Calendar Year 1997:

Salmonella Isolates: 1287 Human, 2391 Veterinary

Calendar Year 1998:

Salmonella Isolates: 1400 Human, 3500 Veterinary

Calendar Year 1999:

Salmonella Isolates: 2000 Human, 4000 Veterinary (target)

Goal Statement: Properly target resources related to education and enforcement initiatives by maintaining the number of follow-up violative tissue residues investigations at 600 in targeted food-producing animals.

Data Sources: Residue Violation Information System (RVIS); Tissue Residue Information Management System (TRIMS)

Baseline Data:

FY 1996: 727 tissue residues

FY 1997: 423

FY 1998: 500 (target)

FY 1999: 600 (target)

Goal Statement: Increase the scientific basis for prioritizing research and surveillance activities by increasing the number of risk assessments performed regarding antimicrobial products to two per year.

Data Sources: CVM's priority project tracking system

Baseline Data:

FY 1999: 1 assessment (target)

Goal Statement: Expand the geographical scope and capacity of the National Antimicrobial Resistance Monitoring System (NARMS) by the establishment of an international resistance database.

Data Sources: FDA-CDC-USDA National Antimicrobial Monitoring Program

Baseline Data:

FY 1999: Develop infrastructure.

Verification and Validation

An integral part of the FDA continual improvement initiative has been an upgrade of our data processing and information systems. This includes automation of manual systems and integration of existing systems which reduces duplication and chances of error due to re-keying of data. Our information and data collection systems contain automatic data checks such as comparisons against lists of "valid" responses for a given data field. By programming "business rules" into our systems, the chance for "human" error is reduced. For example, due dates for applications are appropriately assigned and review time is accurately tracked. Data access is restricted to ensure that only appropriate personnel can enter data, review data, or audit the data. (Checks are in place to ensure that the person who enters the data does not audit the data, etc.)

As part of our commitment to seek input from our stakeholders, we are working with industry to be sure that our pre-approval performance measures are appropriate for our stated goals. We are also working with, and using data from, other governmental agencies such as CDC and USDA. We have established memorandums of understanding and memorandums of need with other agencies to ensure that our data needs are addressed by our federal partners. For example, FDA was fully involved in the design and development of the FDA/USDA Residue Violation Information System (RVIS).

Some of our performance measures required the creation of new data bases to capture the appropriate information and track our progress. For example, in order to accomplish our Food Safety Initiative goals we developed some databases in-house and entered into Interagency Agreements for the development of other databases. We are therefore dependent to some extent on the data validation processes of our sister agencies.

Some of our program work is dependent upon other agencies' planning processes. This is especially true in our illegal residues in meat and poultry program which targets the follow-up of violative tissue residues received from USDA. USDA prepares an annual residue sampling plan with input from FDA. Under the new Hazard Analysis Critical Control Point (HACCP) plan, the requirements that slaughter plants sample has changed substantially. USDA's Food Safety Inspection Service (FSIS) takes some samples, but

only if an animal is suspect. Because the USDA residue plan has changed, it is extremely hard to judge how many residue reports will be sent to FDA for follow-up investigation.

We have also ensured Year 2000 compliance of data applications in software application. The Animal Drugs and Feeds program has been developed in conjunction with the FDA's program of creating an inventory of data applications, analyzing their degree of Year 2000 compliance, and developing a plan to ensure compliance with Year 2000 requirements.

1. ADAA substantially alters the way FDA regulates and approves animal drugs and medicated feeds by granting the authority to exercise considerable flexibility in regulatory decision making. During the implementation phase which includes promulgation of regulations through notice and comment rulemaking, FDA is continuing the dialogue with stakeholders that began prior to the passage of the ADAA.
2. FDAMA initiatives in the Animal Drugs and Feeds Program premarket area requires the Center to accomplish the following: 1) develop guidance regarding the content and review of applications and supplemental applications for approved products; 2) participate in the development of reports and publications required to meet all statutory review requirements by July 1, 1999; eliminating backlogs of applications under review by January 1, 2000; 3) participate in the development of an information system to track the status of applications described in the act; and 4) participate in the development of training and education programs for employees.
3. Figures from the National Academy of Sciences.

MEDICAL DEVICES AND RADIOLOGICAL HEALTH

Total Program Resources (FY 2000):	\$000	FTEs
Center	125,468	1,112
Field	60,583	521
Total	186,051	1,633

Program Overview

FDA's Medical Devices and Radiological Health Program is responsible for ensuring the safety and effectiveness of medical devices and eliminating unnecessary human exposure to man-made radiation from medical, occupational, and consumer products. There are thousands of types of medical devices, from heart pacemakers to contact lenses. Radiation-emitting products regulated by FDA include microwave ovens, video display

terminals, and medical ultrasound, and x-ray machines. FDA accomplishes its mission by:

- reviewing requests to research or market medical devices;
- collecting, analyzing, and acting on information about injuries and other experiences in the use of medical devices and radiation-emitting electronic products;
- setting and enforcing Good Manufacturing Practice regulations and performance standards for radiation-emitting electronic products and medical devices;
- monitoring compliance and surveillance programs for medical devices and radiation-emitting electronic products; and
- providing technical and other nonfinancial assistance to small manufacturers of medical devices.

The FDA Modernization Act of 1997 (FDAMA) requires FDA to conduct more timely and interactive application reviews, improve the quality and timeliness of postmarket surveillance data, expand participation in international harmonization activities, and improve information and education for industry and health professionals. In order to implement these mandates, 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.

Program Strategic Goals

Strategic Goal 1:

Ensure that medical devices intended for human use are safe, effective and properly labeled by assuring that premarket submissions are properly processed within the specified time frames as directed by law.

Resources: \$70,325,000 639 FTEs

Performance Goals:

- Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first actions (within 75 days) completed from 67 percent in FY 1998 to 85 percent in FY 2000 and 95 percent by FY 2002. [\(1\)](#)
This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices
- Review and complete 85 percent of Premarket Approval Application (PMA) supplements for new indications within 180 days in FY 2000 and 95 percent by FY 2002. [\(1\)](#)
- Review and complete 85 percent of complex 510(k) (Premarket Notification) final actions within 90 days in FY 2000 and 95 percent by FY 2002. [\(1\)](#)
- Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days. [\(1\)](#)

- Complete 95 percent of Investigational Device Exemptions (IDE) "Agreement" meetings and Premarket Approval Application (PMA) "Determination" meetings within 30 days. ⁽¹⁾

This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices

Rationale:

Medical devices intended for marketing in the United States are subject to rigorous premarket review by the FDA. Prior to marketing a device, manufacturers must seek FDA safety and effectiveness approval of their products. FDA is responsible for assigning marketed medical devices to a regulatory category (Class I--General Controls; Class II--Special Controls; Class III--Premarket Approval). FDA reviews: 1) Premarket Notifications (510(k)s)-- products substantially equivalent to products on the market; 2) Investigational Device Exemptions (IDEs)--devices used in clinical investigations on human subjects; and 3) Premarket Approval Applications (PMAs)--devices that support or sustain human life, which present a reasonable risk of illness or injury.

To accomplish this premarket responsibility, FDA is charged with review of submissions within the stated time frames specified in the law. FDA strives to support a stable and predictable review process, and meet new statutory FDAMA requirements for reduced review times for PMAs and 510(k)s and increased interactions with sponsors. A performance goal for interactions with sponsors is included and covers IDE Agreement Meetings and PMA Determination Meetings. An IDE Agreement Meeting may be requested by a sponsor prior to submitting an IDE application to discuss specific investigational plans for a Class III or implantable device. A PMA Determination Meeting may be requested by a prospective PMA applicant to determine the type of scientific evidence necessary for PMA approval. These meetings will help to expedite the review process and make medical devices available more quickly.

FDA is focusing the proposed medical device user fee initiative in the budget on three application types: PMAs, PMA supplements, and complex 510(k) applications. Complex 510(k)s include Class III 510(k)s, de novo classifications (a FDAMA process that allows low risk devices found to be not substantially equivalent to be classified by risk rather than automatically assigning them to Class III), and new technologies requiring clinical investigations to determine substantial equivalence. These applications involve potentially high-risk devices that have the highest likelihood of significantly improving the treatment of patients. It is essential that FDA complete the review process for these products quickly and thoroughly.

Growth in the size of the medical device industry and in the complexity of new medical devices will continue to challenge FDA to stay up to date with breakthrough medical devices and to maintain high quality timely reviews, required interactions with industry, and current review guidance. Research and development expenditures by the industry increased 91 percent from 1990 to 1996 with an increase of approximately one billion dollars projected from 1997 to the year 2000. Quantum leaps in device miniaturization, microprocessor software control, artificial intelligence decision support, remote

operation, and drug/biologics/tissue combinations are already revolutionizing medical care. The user fee funding will enable FDA to substantially improve review timeliness for these applications in FY 2000 and to meet statutory timeliness requirements in FY 2002.

There are two goals relating to 510(k)s. One goal is for first actions on 510(k)s within 90 days which deals with the statutory requirement to review a 510(k) within 90 days. The second goal is for final actions within 90 days. This final actions goal responds to stakeholder interest, especially among Congress and the device industry, in having the review completed within 90 days with no further action required.

On June 26, 1996, FDA issued a final rule to carry out provisions of the Safe Medical Devices Act of 1990 regarding humanitarian use devices (HUDs). This regulation became effective on October 24, 1996. An HUD is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. A device manufacturer's research and development costs could exceed its market returns for diseases or conditions affecting small patient populations. FDA, therefore, developed and published this regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

The regulation provides for the submission of an humanitarian device exemption (HDE) application, which is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA. FDAMA established a requirement that FDA review HDEs within 75 days. Beginning in FY 1998, performance data for PMAs also includes data for HDEs. The on-time performance goal for PMAs also includes HDEs.

Approaches, Skills, Technology, and External Factors:

FDA is redirecting resources to high-risk, high-impact product areas where direct intervention helps consumers and health care professionals most. This may increase resources in key areas and decrease resources in areas that pose lower risk to the public or where FDA's direct involvement is not essential. Since premarket approval applications deal with new products, they represent high potential impact on patients; therefore FDA intends to shift more resources to reviewing these products. Although FDA will continue to re-engineer device reviews to make optimal use of resources, the additional requirements involved in starting up FDAMA implementation and for increased interactions with sponsors may impair program performance. With the requested increase in funding for FY 2000, FDA will substantially improve review timeliness and quality in FY 2000 and will meet its major statutory timeliness requirements in FY 2002.

Resources involved in this effort include support from various center organizations: the Office of Science and Technology will perform scientific reviews and assist in establishing standards; the Office of Systems and Management will provide information system support; the Office of Surveillance and Biometrics will provide statistical

reviews; and FDA's Office of Regulatory Affairs will assist with pre-approval inspections and data integrity verification.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first actions (within 75 days) completed from 67 percent in FY 1998 to 85 percent in FY 2000 and 95 percent by FY 2002.

****This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices****

Data Sources: Center for Devices and Radiological Health (CDRH) Premarket Tracking System and Receipt Cohorts

Baseline Data:

<u>PMA's Only</u>	<u>PMA's & HDEs</u>
FY 1996: 51%	Not applicable
FY 1997: 79%	Not applicable
FY 1998: 83% (estimate)	67% (estimate)
FY 1999: 70% (target)	65% (target)

Goal Statement: Review and complete 85 percent of Premarket Approval Application (PMA) supplements for new indications within 180 days in FY 2000 and 95 percent by FY 2002.

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:

FY 1997: 65%
FY 1998: 86% (estimate)
FY 1999: 70% (target)

Goal Statement: Review and complete 85 percent of complex 510(k) (Premarket Notification) final actions within 90 days in FY 2000 and 95 percent by FY 2002.

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:

FY 1996: 65%
FY 1997: 70%
FY 1998: 72% (estimate)
FY 1999: 65% (target)

Goal Statement: Review and complete 95 percent of 510(k) (Premarket Notification) first actions within 90 days.

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:

FY 1996: 94%

FY 1997: 98%

FY 1998: 99.5%

FY 1999: 90% (target)

Goal Statement: Complete 95 percent of Investigational Device Exemption (IDE) "Agreement" meetings and Premarket Approval Application (PMA) "Determination" meetings within 30 days.

****This goal supports the accomplishment of the NPR High Impact Agency goal, Faster Access to Important New Medical Devices****

Data Sources: CDRH Premarket Tracking System and Receipt Cohorts

Baseline Data:

FY 1998: 65% (estimate)

FY 1999: 65% (target)

Strategic Goal 2:

Ensure the safety and effectiveness of facilities that provide mammography services.

Resources: \$21,317,000 147 FTEs

Performance Goals:

- Maintain annual inspection coverage for mammography facilities (8,900 inspections of a total of approximately 10,000 facilities) in FY 2000.
- Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level 1 (serious) inspection problems.

Rationale:

Breast cancer is the most commonly diagnosed non-skin cancer and the second leading cause of cancer deaths among American women. Experts estimate that during the 1990's as many as 1.8 million women will be diagnosed with breast cancer, and 500,000 will die from it. The probability of survival increases significantly, however, when the disease is detected in its early stages. Currently, the most effective technique for early detection of breast cancer is screening mammography, an x-ray procedure that can detect small breast tumors and abnormalities up to two years before they can be detected by touch.

The Mammography Quality Standards Act (MQSA) was signed into law on October 27, 1992, to address the health need for safe and reliable mammography. The Act requires all mammography facilities be certified by the Secretary of Health and Human Services as meeting specific quality standards in the areas of equipment, personnel, quality assurance, record keeping, and reporting. FDA estimates that there are approximately 10,000 mammography facilities that are covered by the MQSA legislation.

The use of mammography as a cancer detection technique is directly related to the quality of mammography procedures. Mammography is one of the most technically challenging radiological procedures and ensuring the quality of the diagnostic image is difficult. If the image is of poor quality, tumors and abnormalities may go undetected. Accurate interpretation of mammograms is equally as important as image quality. A mammogram that is incorrectly interpreted as showing an abnormality could cause a woman to go through unnecessary and costly follow-up procedures, such as ultrasound or biopsies. A false negative reading could result in missed diagnoses and treatment, which could cost a woman's life.

Approaches, Skills, Technology, and External Factors:

The MQSA program is directed to the certification of mammography facilities and to annual inspections to ensure that they remain in compliance with established quality standards. The approaches that FDA uses to assure safe, high quality mammography include setting standards for equipment, personnel and practices: conducting inspections to see if standards are met and image quality is maintained; and educating mammography facilities' employees. FDA conducts its compliance work with state inspectors and accreditation bodies, such as the American College of Radiology. Coordination is also crucial for consumer and health professional educational activities. Almost all certified facilities are inspected each year. In some cases inspections are not completed if facilities are not certified, if there is an ongoing effort to correct problems identified during an inspection, or if facilities go out of business.

Safe and reliable quality mammography is key to implementation of FDA's goals in this area. FDA receives and reviews mammography facility inspection reports and utilizes these to measure performance. Additionally, FDA maintains communication and informs not only industry, medical practitioners but also consumers. The tasks require personnel of multiple disciplines and specialized training plus specialized test equipment to assess mammography safety and effectiveness. One performance goal is to ensure that there are less than 3 percent of facilities with Level 1 or serious problems. These problems generally affect the accuracy of the mammogram itself, specifically the accuracy of the image.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Maintain annual inspection coverage for mammography facilities (8,900 inspections of a total of approximately 10,000 facilities) in FY 2000.

Data Sources: Mammography Program Reporting and Information System (MPRIS)

Baseline Data:

FY 1996: 8,783

FY 1997: 8,280

FY 1998: 9,413

FY 1999: 8,900 (target)

Goal Statement: Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level 1 (serious) inspection problems.

Data Sources: Mammography Program Reporting and Information System (MPRIS)

Baseline Data:

FY 1996: Less than 5% with Level 1 findings

FY 1997: Less than 3% with Level 1 findings

FY 1998: Less than 3% with Level 1 findings (estimate)

FY 1999: Less than 3% with Level 1 findings (target)

Strategic Goal 3:

Improve the detection of problems with medical devices, identify high risk medical devices, and prevent injury by using new reporting systems and procedures.

Resources: \$19,199,000 151 FTEs

Performance Goals:

- Develop Sentinel Surveillance System for injury reporting based on approximately 75 to 90 representative user facilities.
- Develop baseline data to estimate problem and risk magnitude for marketed medical devices.
- Apply improved analytical methodology to approximately 30,000 manufacturer event reports, an increase of at least 20 percent over FY 1999.

Rationale:

No system of premarket review, no matter how thorough, can prevent all potential safety problems once a device is in widespread use. Thus a key element in any comprehensive program to regulate medical devices is postmarket reporting--a system through which FDA receives reports of serious adverse events. Such reporting forms the basis for corrective actions by the Agency, which include warnings to users and product recalls. This is especially true as FDA moves towards less direct involvement in the premarket review of lower-risk devices.

FDA is responsible for monitoring the market for injuries related to medical devices. The major efforts in the postmarket area are focused on the improvement of our ability to detect and analyze medical device problems by focusing on high-risk devices and expanding scientific efforts. FDA received over 63,000 postmarket reports in FY 1998, including mandated reports from medical device manufacturers and user facilities; voluntary reports from medical device professionals received through the problem reporting program (MedWatch); and results of field inspections or investigations.

FDAMA authorizes FDA to discontinue universal user facility reporting and implement a Sentinel surveillance system composed of a network of user facilities that constitute a representative profile of user reports. The user surveillance system currently under development is based on the premise that a select group of highly trained reporting facilities can provide high quality, informative reports that can be representative of user facility device problems in general.

Approaches, Skills, Technology, and External Factors:

FDA is currently managing the huge numbers of reports in three phases. During the first phase, the reports are scanned for completeness and entered into the data management system. During the second phase the reports are analyzed to assess rare versus expected events, seriousness, and public health and vulnerability of the affected population. The final phase focuses on action, such as issuing safety alerts and notifications to users (health professionals and patients) warning them of concerns and advising them how to prevent future occurrences.

FDA believes significant gains can be derived from increased use of summary and alternative reporting, particularly where many reports address the same problems, and where these problems are already well known to FDA and to the user community. Such summary reporting can provide FDA with information about device performance in the aggregate while making it unnecessary to screen so many individual reports. More time can also be devoted to analyzing reports.

FDA has begun the pilot study for a sentinel surveillance system. By using the reports of a cadre of dedicated and trained clinical personnel at participating facilities, the sentinel system has the potential to enhance the validity and reliability of the data submitted, thus affording a higher level of public health protection.

It is also important that FDA have access to baseline or "denominator" data on device usage. This will help the Agency judge the significance of MDR reports, including both the rate at which the problem may be occurring and whether a manufacturer's product is experiencing more or fewer problems than would be expected from its market share. FDA is currently developing a pilot project in conjunction with the industry to assess the feasibility and utility of asking industry to provide the denominator data on their products.

In summary, FDA's postmarket strategy is to improve postmarket reporting by targeting high-risk devices and improving communication with the medical community, more efficient reporting, and better health protection. FDA will also expand the use of tools like summary reporting, particularly where many reports address a well known problem. Sentinel surveillance will be used for high-risk, poorly understood or previously unidentified problems.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Develop Sentinel Surveillance System for injury reporting based on approximately 75 to 90 representative user facilities.

Data Sources: CDRH Adverse Event Reports

Baseline Data:

FY 1998: Recruit 24 pilot facilities

FY 1999: Evaluate pilot efforts

Goal Statement: Develop baseline data to estimate problem and risk magnitude for marketed medical devices.

Data Sources: CDRH Adverse Event Reports

Baseline Data:

FY 1999: Hold small group meeting to discuss problems

Goal Statement: Apply improved analytical methodology to approximately 30,000 manufacturer event reports, an increase of at least 20 percent over FY 1999.

Data Sources: CDRH Adverse Event Reports

Baseline Data:

FY 1998: apply to 16,000 to 20,000 reports (estimate)

FY 1999: apply to 20,000 to 25,000 reports (target)

Strategic Goal 4:

Improve inspection coverage for both domestic and foreign medical device manufacturers and implement the mutual recognition agreement (MRA) with the European Union (EU) for foreign inspections.

Resources: \$49,862,000 448 FTEs

Performance Goals:

- Improve inspection coverage for Class II and Class III domestic medical device manufacturers from 26 percent in FY 1999 to 39 percent in FY 2000.⁽²⁾
- Improve inspection coverage for Class II and Class III foreign medical device manufacturers from 12 percent in FY 1999 to 19 percent in FY 2000.⁽²⁾
- Implement the Mutual Recognition Agreement (MRA) with the European Union (EU).
- Improve quality conformance of high-risk products like cardiovascular devices by committing over 90 percent of inspection resources to high-risk devices.
- Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.

Rationale:

The Compliance program enforces numerous regulations to protect the public from unsafe or ineffective medical devices or radiological products. FDA also informs and verifies that medical device firms are knowledgeable and utilize Good Manufacturing Practices (GMP). Inspections of devices fall into three categories: 1) Routine Surveillance Inspections--to determine compliance with FDA's Good Manufacturing Practices (GMP) Act; 2) Targeted Inspections--for approval to market high risk devices; inspections triggered by adverse reaction incidents; or product recalls; 3) Compliance Inspections--to collect evidence for pending enforcement actions.

Medical devices vary widely in their complexity and their degree of risk or benefits. They do not all need the same degree of regulation. Thus, FDA places all medical devices into one of three regulatory classes based on the level of control necessary to assure safety and effectiveness of the device. These classes are:

Class I --General Controls

Class II -- General Controls and Special Controls

Class III -- General Controls, Special Controls and Premarket Approval

Class I devices are subject to the least regulatory control. They present minimal potential for harm to the user and are often simpler in design than Class II or Class III devices. Examples of Class I devices include elastic bandages, examination gloves, and hand-held surgical instruments.

Class II devices are those for which general controls alone are insufficient to assure safety and effectiveness, and existing methods are available to provide such assurances. In addition to complying with general controls, Class II devices are also subject to special controls. Special controls may include special labeling requirements, mandatory performance standards and postmarket surveillance. Examples of Class II devices include powered wheelchairs, infusion pumps, and surgical drapes.

Class III is the most stringent regulatory category for devices. Class III devices are those for which insufficient information exists to assure safety and effectiveness solely through general or special controls. Class III devices are usually those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.

Although medical devices have become more medically and technologically complex and the device industry is growing domestically and internationally, device and radiological health inspection resources have been reduced by 23 percent since FY 1995. FDA inspected only 28 percent of all 5,248 domestic manufacturers (Class I, II, and III devices) in FY 1997. Of the domestic firms inspected, 13 percent had violations. FDA inspected only 8 percent of all 3,803 foreign manufacturers (Class I,II, and III devices) in FY 1997. Of the foreign firms inspected, 18 percent had violations. The combined domestic and foreign inspection coverage was 20 percent in FY 1997. FDA's inadequate device inspection coverage impairs product safety assurance and impairs FDA's ability to carry out the following responsibilities:

- FDAMA shifts premarket clearance for many low and medium risk devices to postmarket quality systems conformance. Firms may declare conformity to standards or quality systems requirements as part of streamlining premarket clearance. However, FDA will be unable to monitor quality systems conformance at current resource levels.
- Foreign inspection coverage is very low and the mutual recognition agreement implementation with the EU will require extensive training of EU assessment bodies by FDA. FDA cannot maintain foreign inspections or successfully implement the MRA with current resources. In the long term, when the MRA is successfully implemented, it will reduce the number of foreign firms that FDA will need to inspect.
- Emerging device product safety assurance issues will require increased attention. These include enforcing new standards for patient leads and cables, home health care, medical software, latex products and allergic reactions, interventional fluoroscopy, digital imaging, electronic article surveillance, new laser technology, and electronic magnetic interference.

Approaches, Skills, Technology, and External Factors:

FDA is requesting a FY 2000 budget increase to strengthen domestic device product safety assurance and implement quality systems (and support 510(k) conformance). This will be done through state contracts that will also strengthen state medical device expertise. FDA will also strengthen international product safety assurance by increasing foreign inspection coverage and implement the MRA through training EU assessment bodies. The increased inspection coverage for FY 2000 will not meet the long-term objective of inspecting 50 percent of all device manufacturers each year, but will significantly improve product safety and quality systems conformance. The FD&C Act authorizes FDA to inspect all device firms and requires that all Class II and III medical device firms (manufacturers, relabelers, reproducers, etc.) be inspected every two years.

FDA believes that some level of Class I inspections is needed as part of FDA's overall compliance responsibilities.

Three categories have been added to the FDA compliance activities by FDAMA. The first of these new requirements is foreign firm registration. The second category involves technical coordination and communication with foreign governments. The third category is a new requirement to inspect foreign firms. FDA will reallocate resources from within quality assurance to handle these requirements. At the same time, efforts to improve the inspection procedures for domestic firms is underway along with a shift of priorities from low to high-risk devices.

The compliance program is focused on the improvement of enforcement actions by redirecting resources to high-risk devices such as implants. However, limitations on inspection resources have put coverage below critical mass. Annual inspections average seven years, well below statutory requirements. In addition, 510(k) exemptions for Class I products puts more need for Class I inspections to verify that firms have quality systems in place. MRA implementation requires expanded foreign inspections. Finally, compliance activities are providing an opportunity for increased utilization of GMPs by enhancing the body of knowledge and providing more training to field personnel.

During FY 1997, compliance activities have been centered on the development of a risk-based, product-specific system. Appropriate high-risk medical devices to be included in the FY 1999 compliance program are being identified using a newly developed product-risk model. FDA is in the process of redirecting resources to high-risk devices. These devices will receive priority in compliance program planning. Baseline data are being established as the profile of current compliance activity and progress will be measured by comparison of the current profile with a snapshot taken at a future time.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Improve inspection coverage for Class II and Class III domestic medical device manufacturers from 26 percent in FY 1999 to 39 percent in FY 2000.

Data Sources: CDRH Field Data Systems

Baseline Data:

Class II and III domestic manufacturers only:

FY 1997: 40%

FY 1998: 33% (estimate)

FY 1999: 26% (target)

Note about goal: This includes inspections done by FDA directly, or through state contracts or partnership agreements on Class II and III domestic medical device manufacturers. Achievement of this goal relies on the willingness and ability of the states to contract with FDA to inspect a portion of the medical device industry. To implement

these contracts, FDA's experience predicts that a significant investment in training and time is necessary to ensure quality and uniformity of inspections.

Note about baselines: In FY1999, FDA plans to inspect 880 of the 3,429 Class II and III domestic manufacturers, for overall coverage of 26 percent. This is 834 inspections short of the 1,714 required to inspect domestic Class II and III device manufacturers an average of once every two years. Allocation of inspection funding to Class II and III domestic manufacturers will result in none of the projected 3,335 Class I domestic manufacturers being inspected.

Goal Statement: Improve inspection coverage for Class II and Class III foreign medical device manufacturers from 12 percent in FY 1999 to 19 percent in FY 2000.

Data Sources: CDRH Field Data Systems

Baseline Data:

Class II and III foreign manufacturers only:

FY 1997: 23%

FY 1998: 14% (estimate)

FY 1999: 12% (target)

Note on baselines: This includes inspections done by FDA directly or through the mutual recognition agreement with the European Union, on Class II and III foreign medical device manufacturers. In FY 1999, FDA plans to inspect 236 of 2,027 Class II and III foreign manufacturers, for overall coverage of 12 percent. This is 777 inspections short of the 1,013 required to inspect foreign Class II and III device manufacturers an average of every two years.

Allocation of inspection funding to Class II and III foreign manufacturers will result in none of the projected 3,648 Class I foreign manufacturers being inspected.

Goal Statement: Implement the Mutual Recognition Agreement (MRA) with the European Union (EU).

Data Sources: CDRH Field Data Systems

Baseline Data:

FY 1998: Signed the Mutual Recognition Agreement with the European Union

FY 1999: Chairing the Global Harmonization Task Force that seeks to harmonize regulatory requirements

Goal Statement: Improve quality conformance of high-risk products like cardiovascular devices by committing over 90 percent of inspection resources to high-risk devices.

Data Sources: CDRH Field Data Systems

Baseline Data:

FY 1998: 50% of inspection resources devoted to high-risk devices (estimate)

FY 1999: 75% of inspection resources devoted to high-risk devices (target)

Goal Statement: Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.

Data Sources: FDA Field Data Systems

Baseline data:

FY 1997: 93%

FY 1998: 93%

FY 1999: at least 90% (target)

Note about goal: Conformance rates estimate the post-inspection status of the establishments inspected in the given year. They are based on the number of establishments inspected, the incidence of serious deficiencies detected (Official Action Indicated), and statistical data of deficiency corrections. Since firms inspected are not randomly selected from the entire population, the rates should not be applied across that population. However, as coverage of the inventory of firms is improved, the rates will better represent the overall status of the industry sector.

Strategic Goal 5:

Provide science-based medical device and radiological product quality assurance, including recognizing over 450 standards for use in application review.

Resources: \$14,374,000 137 FTEs

Performance Goals:

- Update list of recognized standards.
- Investigate correlation of device failures with aging biomaterials and provide quality assurance for device software.

Rationale:

FDA's goal is to provide science-based device product safety assurance to the public. Science, technology and standards activities are directed to improve science support related to the device review process. FDAMA requires FDA to recognize and use standards in the application review process. FDA plans to expand its participation in international harmonization of standards. Additionally, FDA plans to increase the use of consensus standards developed by such national and international organizations as the

American Society for Testing and Materials and the International Standards Organizations to improve premarket approval times.

Approaches, Skills, Technology, and External Factors:

Resources are being utilized to increase participation of science expertise in the review and approval of high-risk medical devices during premarket review. In addition, efforts are underway to develop and promote consensus performance standards as guides of safer and more effective medical products and to enhance the quality of regulatory decision making.

Under this approach, FDA would identify in guidance documents those standards that may address aspects of a substantial equivalence determination, such as specified testing. Manufacturers would certify that their devices met the standards, and submit that certification to the Agency in lieu of the underlying data. Manufacturers would retain the option of taking alternative approaches and submitting the underlying data to FDA. In most cases a given standard would address only some aspects of a substantial equivalence determination for a particular device, but there may be instances where a standard or combination of standards would address all aspects of a 510(k) decision.

FDA needs to update test methods, product standards, quality assurance techniques and other scientific tools needed for science-based product quality testing and regulation of marketed devices. FDA needs to develop the following tools to promote public health by assuring that marketed devices are safe and effective, and in operation in the year 2000:

- Correlation of device failures with accelerated aging of polymeric biomaterials
- Quality assurance techniques for device software for small manufacturers
- Support user participation in high priority test methods and product standards

FDA will target laboratory support to guide standard setting and harmonization, keep review up-to-date, and consult on review of emerging technologies. Specifically, FDA should target lab work to support review standards, update guidance and risk assessments, and build the science base to consult on product reviews. FDA will do laboratory work to support application in the following areas:

- Information management;
- Computer assisted diagnosis; and
- Devices for minimally invasive procedures.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Update list of recognized standards.

Data Sources: Standard status document reports

Baseline Data:

FY 1997: 2 standards recognized

FY 1998: 370 standards recognized

FY 1999: Recognize more than 415 standards (target)

Goal Statement: Investigate correlation of device failures with aging biomaterials and provide quality assurance for device software.

Data Sources: CDRH FDA laboratory documentation

Baseline Data:

FY 1998: Identify priority materials for standard development.

FY 1999: Initiate standards development.

Strategic Goal 6:

Assure that the potential of radiation to benefit the public can be realized at a minimum risk of harm.

Resources: \$10,974,000 111 FTEs

Performance Goal:

- Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95 percent of identified high-risk, noncompliant or defective products within 30 days of discovery.

Rationale:

Under the Radiation Control for Health and Safety Act (RCHSA), FDA conducts an electronic radiation control program to assess the biological effects resulting from all types of radiation exposure, evaluates radiation emissions from electronic products, conducts research to minimize exposure, and sets and enforces radiation performance standards. Manufacturers of radiation-emitting products such as x-ray machines, lasers, microwave heating equipment, television and ultrasonic therapy equipment are required to submit initial reports, annual reports, and model change reports to FDA.

Approaches, Skills, Technology, and External Factors

The RCHS program is focused on assuring minimal exposure to radiation from electronic products by assessing emissions, labeling, controls and user practices. Safety of use is improved through enhancing the body of knowledge and providing information to industry, researchers, consumers and medical practitioners. As technology progresses the scope of products increases much faster than the knowledge of bioeffects. Adverse event reports are monitored for use in adjusting priorities. Interpretive policies are developed to permit greater flexibility in meeting requirements that are not critical to radiation safety.

The task of implementing the Radiation Safety and Control Act is difficult because of emerging technologies and the need to inform not only industry, medical practitioners but also consumers. The tasks require personnel of multiple disciplines and specialized training plus specialized test equipment to assess bioeffect safety and effectiveness. FDA presents recommendations to an advisory committee prior to publication in the *Federal Register*.

In conjunction with its regulatory efforts, FDA carries on specialized programs to reduce patient exposure during diagnostic x-ray procedures by encouraging improved practice among health professionals and by developing new x-ray techniques. FDA makes continual checks to assure that the potential of radiation can be realized at a minimum risk of harm. As new radiation-producing electronic products are developed, FDA evaluates them to ensure they are safe.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95 percent of identified high-risk, noncompliant or defective products within 30 days of discovery.

Data Sources: CDRH Tracking Data, FDA and state laboratory guides, recall files and Inspection reports

Baseline Data:

FY 1996: 95%

FY 1997: 95%

FY 1998: 95% (estimate)

FY 1999: 95% (target)

Verification and Validation

To help ensure Agency consistency in tracking and reporting premarket activities, the Medical Device Program utilizes the Premarket Tracking System which contains various types of data taken directly from the premarket submissions. FDA employs certain conventions for monitoring and reporting performance; among these are groupings of premarket submissions into decision and receipt cohorts. Decision cohorts are groupings of submissions upon which a decision was made within a specified time frame, while receipt cohorts are groupings of submissions that were received within a specified time frame. Descriptive statistics relating to application processing time frames are used to monitor performance.

The Mammography Program Reporting and Information System (MPRIS) is a set of applications used to support all aspects of the FDA implementation of the Mammography Quality Standards Act of 1992. This includes the collection, processing and maintenance of data on mammography facility accreditation, certification, FDA inspections and compliance actions. MPRIS is envisioned as a centralized repository of information that

supports FDA's mission to improve the quality of mammography and improves the overall quality, reliability, integrity, and accessibility of facility certification, inspection, and compliance data by eliminating multiple versions of the data while expanding and automating data edits, validation, and security of a single integrated database.

The medical device postmarket adverse event reporting system was the subject of a General Accounting Office report in January 1997 which raised some concerns about FDA's ability to process reports and provide an early warning system. FDA has been working to improve the system. The major problems are the large volume of the reports received, the accuracy of and necessity of many reports, and the ability to quickly process the reports. In some cases, liability concerns on the part of medical professionals and facilities may affect what they report. FDA is developing and testing a new sentinel system which would rely on reporting from a select and representative sample of user facilities.

A data concern of the medical device and radiological health compliance program is identifying foreign firms which are subject to new registration and inspection requirements. FDA will be working with foreign governments and the European Union in implementing these requirements.

1. Achievement of this performance goal target level is dependent upon passage of User Fee legislation and establishment of management systems to implement user fees by the beginning of FY 2000.
2. There will be no routine coverage for Class I manufacturers.

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

Total Program Resources (FY 2000):	\$000	FTEs
	33,679	227

Program Overview

The National Center for Toxicological Research (NCTR) is responsible for conducting peer-reviewed research that provides the basis for FDA to make sound science-based regulatory decisions, and to promote the health of the American people through enforcement and compliance. NCTR achieves its mission by conducting fundamental and applied research designed to define the biological mechanisms of action underlying the toxicity of products regulated by the FDA. Specific aims of NCTR's research are to understand critical biological events in the expression of toxicity; to develop methods to improve assessment of human exposure, susceptibility, and risk; and to apply these

scientific findings to FDA's premarket application review and product safety assurance efforts.

New technologies have enhanced scientific assessment capabilities. The challenge to NCTR and FDA as a whole is to apply these new technologies where appropriate to detect risk, ensure safety of FDA-regulated products, and to act in the best interest of the public. The FDA has expedited drug, device and biologic approval procedures to provide needed therapies to consumers more quickly. Research results that improve the ability of FDA reviewers to evaluate product safety more rapidly and to estimate human risks more accurately are vital to carrying out the Agency's consumer protection mission. The development of international trade alliances has increased the need to defend regulatory decisions. To accomplish this, the FDA will require strong scientific capability and support.

Financial constraints and increases in the FDA's workload have increased the demand for more efficient, more rapid, and more economical test methods for assessing human risk in FDA headquarters and field laboratories. To respond to these challenges, the National Center for Toxicological Research will continue to support the Agency's overall strategy by maintaining a high-quality, cost-effective research program that is responsive to the Agency's regulatory needs and supports FDA's ability to provide the desired level of consumer protection. NCTR will strive to find better and more economical means of protecting consumers and will focus its research efforts on the highest priority Agency issues. NCTR will continue to leverage research resources through partnerships with other federal agencies, national and international organizations, universities, and industry to best meet Agency needs.

NCTR's research program focuses on three strategic goals that support the Agency's mission to promote public health:

- Develop new strategies for the prediction of toxicity
- Develop computer-based systems that predict human toxicity
- Conduct method-, agent-, and concept-driven research

The first strategic goal, develop new strategies for the prediction of toxicity, addresses the rapid evolution of scientific knowledge. As a science-based agency, FDA must maintain a core of scientific knowledge, skills, and talents to react to new regulated products that are reaching the market. NCTR is developing new predictive systems that will provide the use of state-of-the-art information technology in answering difficult regulatory questions more quickly and with fewer resources. NCTR's new strategies for predicting toxicity include using new test systems that are based on understanding the product's mode of action, refining new and existing tests, as well as conducting studies that help reduce the uncertainty of extrapolating laboratory animal data to humans. Predictive systems will support FDA decisions about toxicity and will guide the design and set priority of subsequent toxicity studies.

The second strategic goal, develop computer-based predictive systems, is an ongoing effort to extend the predictive value beyond an individual set of data. We envision that by placing an accumulation of scientific data into a computer-based predictive system, we might predict the toxicity of a drug or chemical in humans and animals based solely on its structure and/or activity. A system of this nature may reduce the approval time for estrogen-mimicking drugs used for breast cancer treatment or hormone replacement therapy.

The method-, agent-, and concept-driven strategic goal addresses the constant need for evaluating new technology and for revising existing methodology to meet the new regulatory challenges. NCTR will continue to collaborate and consult with scientists from FDA product centers and the Office of Regulatory Affairs in conducting agent-, method-, and concept-driven research to support the expanding regulatory focus of the FDA. Agent-driven research will focus on providing data not available from manufacturers or the scientific literature on specific agents, such as anti-estrogens, neurotoxins, food contaminants, and aquaculture therapeutics. Method-driven research will focus on developing and applying new toxicologic and analytical test methods for more rapid, yet sensitive detection of bacterial pathogens and toxins in food and drugs and decomposition in seafood. NCTR is actively pursuing improved animal bioassay methodology and is supporting the Food Safety Initiative with powerful, state-of-the-art analytical techniques.

Program Strategic Goals

Strategic Goal 1:

Develop new strategies for the prediction of toxicity.

Resources: \$16,645,000 114 FTEs

Performance Goals:

- Develop a new biological assay to measure genetic change and validate two existing models that predict human genetic damage.
- Conduct molecular epidemiology studies to identify biomarkers of the most frequently occurring cancers in highly susceptible subpopulations.
- Develop partnerships with government, industry, and academic scientists to conduct studies that demonstrate cross-species comparability and eliminate assumptions necessary for extrapolating laboratory toxicity data to human disease.

Rationale:

One of the Agency's and NCTR's highest priorities is to increase the ability of FDA reviewers to evaluate and predict rapidly and accurately the adverse effects FDA-regulated products may have on humans. This capability is critical to the Agency's ability to carry out its mission of ensuring the safety and efficacy of FDA-regulated products during the premarket application review process. The human response to a toxic agent is a complex process. To adequately predict the adverse effects of human exposure to a toxic agent, a group of tests must be developed, validated, and applied. NCTR uses a

multi-disciplinary approach to predict human toxicity and evaluate human risk using appropriate animal and non-animal models.

Toxicologic research, often long-term and animal intensive, has traditionally sought to understand the toxicity of chemicals through animal and cell culture exposure. Toxicologic data resulting from such studies have been used to predict risk to humans. The science of toxicology is moving away from its dependency on whole animal test systems that use large numbers of animals and seek relatively few endpoints. Although extrapolation from animal models to humans has been helpful, animal models have their limitations. Increasing evidence points to a need to identify and protect susceptible subpopulations of people at higher risk from exposure to drugs, contaminated food, or other regulated products. In addition, the emphasis of toxicologic research has shifted from descriptive studies to studies that are designed to gain a better understanding of the biological mechanisms underlying the effects of a toxic agent.

NCTR will use transgenic rodents (such as those carrying critical reporter genes) and human cell lines to predict human toxicity. NCTR researchers are continuing to develop laboratory methods that closely mimic human genetic response and predict human genetic damage. Use of the neonatal mouse assay will provide information about the toxicity of agents in a developing animal, information not provided by the more traditional studies in adult rodents. Moreover, traditional studies in adult rodents take longer and are much more costly than those conducted in the neonatal mouse assay. Other NCTR programs use human data to understand the mechanisms of carcinogenesis particularly as they are related to individual susceptibility. Human studies are conducted by our scientists in collaboration with peers at the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research, other agencies (for example, the Environmental Protection Agency, the National Institute for Environmental Health Sciences (NIEHS), and the National Toxicology Program (NTP)), universities, and medical centers around the world. International collaborative studies exploring human biomarkers will help to identify and potentially screen subpopulations at higher risk for developing certain types of cancer. This will improve FDA's ability to determine and ultimately manage risk both in the United States and in collaboration with regulators and scientists throughout the world.

A single approach for risk assessment of both cancer and non-cancer health outcomes is an important goal for FDA's risk assessment staff. Existing cancer and non-cancer as well as neurotoxicological databases are being examined by FDA centers and are useful in helping to predict a broad spectrum of human risk. A new emerging project in the risk assessment area involves determining human risk from foodborne pathogens. Analytical techniques are being used to identify strains of bacteria that are gaining antibiotic resistance. This work is being proposed under the Food Safety Initiative.

Approaches, Skills, Technology, and External Factors:

To achieve this strategic goal, the Center will pursue a multi-disciplined toxicity assessment approach. Information technology will help evaluate human models and

monitor neonatal mouse studies. To accomplish these performance goals, a strong collaborative effort must continue to be fostered within the Agency and external partnerships must be encouraged, established, and maintained. Communication between scientists and reviewers will ensure that complex scientific issues are addressed quickly and that critical data are available to regulators.

Over the next five years, NCTR will face external factors embodied in an environment characterized by scientific challenges, continued advances in science and technology, increasingly complex regulatory challenges, global competition, and a need to protect public health. NCTR will apply new technologies where appropriate to detect risk, ensure safety of FDA-regulated products, and to act in the best interest of the public.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Develop a new biological assay to measure genetic change and validate two existing models that predict human genetic damage.

Data Sources: NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings, manuscripts prepared for publication in peer-reviewed journals.

Baseline Data:

FY 1996:

Evaluated reporter gene systems (Big Blue Transgenic Rat and *hprt* gene) as models for measuring genetic damage.

FY 1997:

Conducted genetic screening and evaluated additional toxicity study results (e.g., cell death and mutagenesis) in relationship to DNA biomarkers of damage.

FY 1998:

Utilized model animal and cell culture transgenic systems to evaluate risk to the human genome.

FY 1999:

Predict adverse human response to regulated products using model transgenic systems.

Goal Statement: Conduct molecular epidemiology studies to identify biomarkers of the most frequently occurring cancers in highly susceptible subpopulations.

Data Sources: NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings, manuscripts prepared for publication in peer-reviewed journals.

Baseline Data:

FY 1996:

Developed world-wide collaboration effort to measure biomarkers of cancer.

FY 1997:

Initiate studies to evaluate the use of molecular biomarkers in clinical studies and identify

subpopulations at increased risk.

FY 1998:

Conducted case-control molecular epidemiology studies to assess breast and prostate cancer in African-American women/men.

FY 1999:

Identify subpopulations of humans at increased risk using molecular markers.

Goal Statement: Develop partnerships with government, industry, and academic scientists to conduct studies that demonstrate cross-species comparability and eliminate assumptions necessary for extrapolating laboratory toxicity data to human disease.

Data Sources: NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings, manuscripts prepared for publication in peer-reviewed journals. Number of government inter-agency agreements, industrial cooperative research and development agreements, and academic grants initiated.

Baseline Data:

FY 1996:

Developed in conjunction with government regulators an approach to safely assess carcinogenic, reproductive, developmental, neurological, genetic and acute toxicology endpoints.

FY 1997:

Risk assessment strategy was reviewed by an outside group of experts from academia and industry.

FY 1998:

Presented, at a scientific forum, a unifying approach to safety assessments for both carcinogenic and non-carcinogenic effects. This addressed the uncertainty caused by extrapolating from high to low dose, from animals to humans, and from route and duration of exposure involved in estimating risk and setting acceptable exposure levels.

FY 1999:

Utilize risk assessments quantifying uncertainty in regulatory decisions.

Strategic Goal 2:

Develop computer-based systems that predict human toxicity.

Resources: \$4,714,000 32 FTEs

Performance Goal:

- Validate a model computer-based predictive system to support and expedite product review of estrogenic or estrogen-like compounds.

Rationale:

An Agency-wide need, as identified by the FDA Senior Science Council, was the application of unique computer-based predictive systems to aid in assessing human toxicity to optimize non-clinical and clinical predictability. FDA reviewers face an ever-increasing quantity and complexity of data in new drug and product applications. Clearly, tools that can provide reviewers quick access to relevant scientific information and a capability for predicting toxicity would expedite review decisions. NCTR, in consultation with other FDA centers, government agencies and industries, is developing a computer-based predictive system that will predict the toxicological activity of a compound by using biological indicators of damage, chemical structures via molecular modeling, and advanced mathematical and computational tools.

This strategic goal contains a single performance goal: to validate a model computer-based predictive system to support and expedite product review. Data developed at NCTR on the toxicity of estrogen and antiestrogen compounds are being coupled with data obtained through scientific collaborations (government, industry and academic) and published in the literature and is being incorporated into a learning set for predictive computations. NCTR is adapting statistical techniques and applied computational techniques to construct this model system.

Approaches, Skills, Technology, and External Factors:

The Agency will need to maintain a strong scientific computing capability to devise better tools to facilitate product approval. NCTR will use Center and on-site contractor resources (FTEs and dollars) from analytical chemistry, computational science, neurotoxicology, and genetic and reproductive toxicology to achieve this performance goal. The Center has an on-site information technology capability that provides expertise in molecular modeling, structure activity relationships, 3-dimensional chemical structure and the selection and acquisition of hardware and software for future developments and improvements. The novelty of this approach is the union of several disciplines focused on a common goal.

External factors that impact this goal include the lack of sufficient data to establish an adequate computer learning set and the lack of routine communication channels through which researchers and reviewers foster internal cooperation. Fluid lines of communication must exist between NCTR, FDA Product Centers, and ORA, between scientists within the various centers and field organizations, and between senior level managers throughout the Agency. This is a particularly daunting challenge since NCTR is located a considerable distance from FDA Headquarters and from many of the field operations. To overcome this challenge NCTR has developed new channels of communications to verify and validate the relevance of our research and to ensure the performance goals are achieved.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Validate a model computer-based predictive system to support and expedite product review of estrogenic or estrogen-like compounds.

Data Sources: Use of prototype computer-based predictive system by FDA reviewers and other government regulators; NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings; and manuscripts prepared for publication in peer-reviewed journals.

Baseline Data:

FY 1996:

Computer hardware and software were procured and installed and systems integration was completed.

FY 1997:

Prototype presented at FDA Science Forum.

FY 1998:

Computer-based predictive system was used to develop model for rodent and human hormone binding proteins.

FY 1999:

Computer-based predictive systems being used to evaluate toxins.

Strategic Goal 3:

Conduct method-, agent-, and concept driven research.

Resources: \$12,320,000 81 FTEs

Performance Goals:

- Conduct studies that relate how a compound causes damage to the damage itself, in order to strengthen the scientific basis for regulation of compounds of FDA significance.
- Develop methods of predicting, more quickly and accurately, the risk associated with foodborne pathogens.

Rationale:

Most regulatory research begins as a precise exploration of a specific agent, a concept, or the use of a particular method. Once techniques are developed, these novel approaches can be applied to answer compelling questions of human health and safety. This goal includes three performance goals that address the Agency strategy of developing science-based product and process standards.

Agent-driven research supported through an interagency agreement with the NIEHS/NTP has permitted NCTR to enhance the rodent bioassay to include the use of studies based on mechanisms of toxic action to improve bioassay interpretation and potentially speed up product review. Currently, NCTR is conducting special studies on four compounds of special concern to FDA: chloral hydrate, fumonisin B₁, malachite green, and urethane in the presence of alcohol. Work is underway to develop testing protocols and facilities to evaluate the harmful effect of skin exfoliants, such as alpha hydroxy acids. NCTR has started long-range multi-generation studies of compounds that disrupt normal endocrine

function. These studies are designed to provide data on how estrogens and anti-estrogens may affect the developing fetus.

The Agency's need for state-of-the-art quantitative identification of toxic agents to strengthen the Agency's postmarket assurance is the basis of NCTR's method-driven research effort. In collaboration with FDA's Center for Food Safety and Applied Nutrition (CFSAN), and as part of the Food Safety Initiative, NCTR is developing methods to identify markers of toxicity in foodborne pathogens and to assess whether these microorganisms are undergoing change, thus becoming more virulent.

Research within this goal capitalizes on partnerships with other FDA centers and with other agencies such as NIEHS and the United States Department of Agriculture (USDA). Regular meetings of scientific experts are held to develop a consensus on the best approach to take in improving the science-based process for the Agency.

Approaches, Skills, and Technology, and External Factors:

To accomplish these goals, NCTR needs continued review and input by other FDA centers, the Office of Regulatory Affairs, and outside experts to encourage and promote FDA-relevant research. National Toxicology Program studies require NCTR to maintain an accredited animal facility that includes a quality assurance staff, pathology capabilities, computerized record keeping, and high-quality animal husbandry and diet preparation support. The scientific expertise to support these goals range from analytical chemists to microbiology to biochemistry, molecular biology, neurotoxicology and biometry.

Externally, market pressures make the pursuit of more sensitive methods undesirable due to impact on profit. NCTR is working in partnership with industry and academia to provide safe and effective detection methods for regulated products by using technology transfer and applying new technologies to existing methods.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Conduct studies that relate how a compound causes damage to the damage itself, in order to strengthen the scientific basis for regulation of compounds of FDA significance.

Data Sources: Evidence that mechanistic data are used in the regulatory process; NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings; and manuscripts prepared for publication in peer-reviewed journals.

Baseline Data:

FY 1996:

Toxicity studies were initiated on two new compounds of interest to FDA, malachite green, an antimicrobial product, and urethane, a beverage contaminant.

FY 1997:

Comprehensive mechanistic studies on FDA-nominated potential carcinogens include complete dosing regimen for two year chronic bioassay on chloral hydrate and fumonisin B₁. Range finding studies on genistein, methoxychlor and nonylphenol were completed and data are being analyzed for toxic effects. Phototoxicity assessment of alpha hydroxy acids was nominated for study.

FY 1998:

Report needed to regulate fumonisin B₁ exposure in foods and long-term chloral hydrate usage completed. Began multi-generation studies of endocrine disrupters.

FY 1999:

Continue two-year chronic bioassays on urethane in ethanol and malachite green. Begin studies to assess risk of alpha hydroxy acids and endocrine disrupters.

Goal Statement: Develop methods of predicting, more quickly and accurately, the risk associated with foodborne pathogens.

Data Sources: NCTR Project Management System; peer-review through FDA/NCTR Science Advisory Board, presentations at national and international scientific meetings; and manuscripts prepared for publication in peer-reviewed journals.

Baseline Data:

FY 1996:

Used novel technology to identify 11 foodborne pathogens.

FY 1997:

Developed, in conjunction with other government agencies, a new protein-based mass spectral technique to identify virulent strains of bacteria.

FY 1998:

Screened animal products and environments for microorganisms harboring antibiotic resistance.

FY 1999:

Evaluate the mechanisms of competitive exclusions as a technique to protect poultry products and explore dose-response models for assessing risk due to pathogenic exposure.

Verification and Validation

As a research component of the FDA, the National Center for Toxicological Research provides peer-reviewed research that supports the regulatory function of the Agency. To accomplish this mission, it is incumbent on the Center to solicit feedback from its stakeholders and partners, which include other FDA centers, other government agencies, industry, and academia. The SAB is composed of non-government scientists from industry, academia, and consumer organizations. This board is further supplemented with subject matter experts and scientists representing all of the FDA product centers. Programs described under each Performance Goal are evaluated at least once every five years by the SAB.

Research proposals are also monitored through partnerships with other scientific organizations. Scientific and monetary collaborations include inter-agency agreements with other government agencies, Cooperative Research and Development Agreements and technology transfer with industry, and grants or informal agreements with academic institutions.

NCTR uses several strategies to ensure the quality of its research and the accuracy of data collected in specific research studies. Study protocols are developed by principal investigators in collaboration with FDA product centers. Findings are recorded by and verified by internal and external peer review. Statistical analyses are performed by the principal investigator and reviewed by members of the Biometry Staff. The analytic approach is checked by different members of the scientific staff and the Deputy Director for Research to verify the scientific integrity of the data.

To ensure that the performance data are accurate and timely, the NCTR Planning and/or the Quality Assurance Staff uses a project management system and reviews to monitor research at the project level on a quarterly basis. NCTR's computer-based project management system is capable of tracking planned and actual resource expenditures for research projects in all three program strategic goals and in the performance goals. Accomplishments and goals are published annually in the NCTR Research Plans and Accomplishments document. Publications reporting research findings are tracked by project, and final reports are archived and distributed to interested parties. Over the past four or five years, NCTR has published yearly over 250 research documents, manuscripts, book chapters, and abstracts in recognized scientific journals.

NCTR's research is also evaluated by other scientists when research findings are presented at national and international scientific meetings and published in peer-reviewed scientific journals. Many of these meetings are sponsored or co-sponsored by NCTR scientists. The scientists make over 500 presentations and invited speeches a year at local science seminars and at national and international meetings. Many NCTR scientists also serve on international scientific advisory boards.

TOBACCO

Total Program Resources (FY 2000):	\$000	FTEs
	68,000	40

Program Overview

Smoking is the leading preventable cause of death in the United States. Every year, another one million young people become regular smokers and one-third of them will

eventually die prematurely as a result of their smoking. The average teenage smoker starts smoking at 14 ½ years of age and becomes a daily smoker by the age of 18.

Tobacco products are responsible for more than 400,000 deaths annually due to cancer, respiratory illness, heart disease, and other health problems. According to the Centers for Disease Control and Prevention (CDC), health care costs associated with smoking soared to more than \$50 billion in 1993.

The Tobacco Program seeks to promote and protect the health of our nation's youth by reducing the number of young people who begin to use and become addicted to tobacco products each year. FDA's long-term goal is a 50 percent decline in young people's use of tobacco within seven years of program implementation. To help reach this goal, FDA will work with other organizations within the Department of Health and Human Services (DHHS) such as the Substance Abuse & Mental Health Services Administration (SAMHSA), CDC, and the National Cancer Institute (NCI).

FDA's role is threefold: enforcement and evaluation, compliance outreach, and product regulation. FDA's overall goals are to reduce the access and appeal of tobacco products to young people, to enlist retailers' and other stakeholders' assistance in these efforts, and to develop regulatory procedures for cigarettes and smokeless tobacco products. FDA's efforts are supported by and coordinated with activities in other agencies within DHHS. For example, SAMHSA uses its authority to withhold substance abuse grants to states that do not achieve required access compliance rates by retailers and also conducts surveys to gather information about tobacco use. CDC's Office of Smoking and Health is primarily involved with public education, research, and surveys. Finally, NCI is also involved in research and education programs. FDA will utilize data gathered by these agencies to both carry out and evaluate its tobacco program. FDA will also work closely with state governments, especially in its enforcement role. The ultimate goal of these combined and coordinated efforts will be a significant reduction of tobacco use by young people.

On April 25, 1997, the District Court in Greensboro, North Carolina, ruled that FDA has jurisdiction under the Federal, Food, Drug and Cosmetic Act (FD&C Act) to regulate nicotine-containing cigarettes and smokeless tobacco as drug delivery devices. The Court upheld all restrictions involving youth access and labeling and struck down, as unsupported by statutory authority, the Agency's advertising restrictions. The Court stayed implementation of all provisions, except those involving age and ID, pending appeal. Appeal was taken and oral argument was held in August 1997 and reargued on June 9, 1998 in the Fourth Circuit Court of Appeals. On August 13, 1998, the Fourth Circuit issued its decision, finding the FDA's assertion of jurisdiction and issuance of regulations invalid. The government is seeking review of this decision by the Supreme Court. Pending the Supreme Court's review (or decision not to hear the case), the Court of Appeals' mandate is stayed and the Agency is continuing to enforce the age and ID provisions.

Program Strategic Goals

Strategic Goal 1:

Reduce the easy access to tobacco products and eliminate the strong appeal of these products to children.

Resources: \$42,000,000 29 FTEs

Performance Goals:

- Conduct 400,000 compliance checks and select certain sites to target for intensified enforcement efforts to determine the effectiveness of different levels of effort.
- Conduct follow-up compliance checks of 100 percent of retailers found to be in violation of the rule.
- Ensure the elimination of certain forms of advertising, especially outdoor advertising within 1000 feet of schools and playgrounds (including transit advertising) and specialty item distribution such as hats and tee shirts with tobacco logos.

Rationale:

To achieve a reduction in the addiction to and death from the use of tobacco products by young people, FDA's rule attempts to limit the availability and appeal of tobacco products to young people. The rule limits the access that young people have to tobacco products by setting a minimum age of purchase at 18, requiring that retailers check a photo identification of all customers under the age of 27 when purchasing tobacco, banning self-service and vending machine sales, and banning free samples. The rule would limit the appeal of these products by imposing stringent restrictions on most advertising media including banning outdoor advertising within 1000 feet of schools and public playgrounds, limiting most print advertising to a black and white text only format, banning all non-tobacco items identified with a tobacco brand and banning brand name sponsorship of sporting and entertainment events.

Approaches, Skills, Technology, and External Factors:

FDA enforces the access restrictions currently in effect primarily through the commissioning of state and local regulatory officials, who conduct unannounced purchase attempts using young people under the age of 18. In FY 2000, the Agency intends to expand its enforcement efforts to have commissioned agents inspect every identified retail outlet at least once every other year (assuming there are 500,000 retailers) and reinspect each violative retailer within three months after notifying the retailer of the violation or after adjudication of civil money penalty. The Agency also intends to establish its own enforcement program in those states that are unable or unwilling to contract with the Agency. If all provisions of the rule are in effect, FDA will also check retailer compliance with the prohibitions against self-service displays, vending machines and certain types of advertising.

Under the current enforcement plan, retailers who do not sell tobacco products to the minor receive a letter informing them that they are in compliance with the rule. Those who do sell to the minor receive a letter informing them that they have violated the rule, and that another compliance check may occur in the near future. If on the second purchase attempt the retailer sells to the minor, the Agency seeks a \$250 civil money penalty. Penalties escalate for subsequent violations of the access restrictions in effect: third violation-\$1500; fourth violation- \$5000; fifth violation- \$10,000. In FY 1999, FDA began investigations of retailers who have been found to have already violated the rule twice. The Agency anticipates seeking civil money penalties for third violations within the first quarter of FY 1999. A penalty schedule for violations of other portions of the regulation will be developed when these provisions go into effect.

In FY 2000, the Agency intends to expand its enforcement program by inspecting 400,000 retailers each year, as opposed to the 200,000 inspected yearly with FY 1998 and FY 1999 money. Because the Agency is unable to inspect all known retailers each year, it will use some of its FY 2000 budget to create targeted demonstration-enforcement areas. Although the vast majority of inspections will be distributed randomly within each state, the targeted demonstration areas will be subject to more intense outreach and enforcement efforts in an attempt to measure the effectiveness of different mixes of interventions and levels of effort on sales of tobacco products to minors. These projects will allow the Agency to plan for more effective use of its enforcement dollars in the future. In addition, assuming other parts of the tobacco regulation are in effect, the Agency will increase the investigators' responsibilities during each check to include checking on the removal of vending machines and self-service displays and illegal advertising. Fewer compliance checks will result if the additional provisions of the rule go into effect because longer and more complicated checks will be required.

The Agency has begun analyzing methods to monitor industry compliance with the restrictions on advertising even though these provisions are not yet in effect. For example, the tobacco rule prohibits all outdoor advertising within 1,000 feet of schools and playgrounds, as measured from the perimeter of the property. FDA has looked at satellite or computer mapping technology as an aid in determining the appropriate 1000-foot area around schools and public playgrounds. This technology can then be made available to state and local government agencies as well as to private groups who can report violations to FDA. Similarly, the tobacco rule requires that all advertising appear in black and white text-only format except in publications read primarily by adults, as measured by a percentage and gross number of adult readers. FDA has met with industry officials in an attempt to identify an appropriate methodology for measuring adult and youth readership of publications.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Conduct 400,000 compliance checks and select certain sites to target for intensified enforcement efforts to determine the effectiveness of different levels of effort.

Data Sources: FDA Tobacco database

Baseline Data:

FY 1997:

Conducted 6,464 compliance checks under a pilot program in 10 states (about 1.3% to 2.6% of the estimated 500,000 to one million retailers of cigarettes and smokeless tobacco products).

FY 1998:

FDA conducted approximately 39,439 compliance checks in FY 1998 and contracted to have approximately 189,000 compliance checks performed by September 1999 with FY 1998 funding.

FY 1999:

In FY 1999, the FDA will contract to have 200,000 compliance checks performed. In FY 1998, FDA entered into contracts with 41 states, the District of Columbia and the Virgin Islands. FDA will use federal investigators to perform the compliance checks in any state that does not sign a contract with the Agency.

Goal Statement: Conduct follow-up compliance checks of 100 percent of retailers found to be in violation of the rule.

Data Sources: FDA Tobacco database

Baseline Data: Baseline data is being developed as the compliance check program is being implemented.

Goal Statement: Ensure the elimination of certain forms of advertising, especially outdoor advertising within 1000 feet of schools and playgrounds (including transit advertising) and specialty item distribution such as hats and tee shirts with tobacco logos.

Data Sources: Federal Trade Commission industry-wide data on advertising expenditures

Baseline Data:

Dollars spent on advertising:

Cigarette advertising, 1996:

Specialty item distribution: \$544,345,000

Outdoor: 292,261,000

Transit: 28,865,000

Total: \$865,471,000

Smokeless tobacco advertising, 1995:

Distribution bearing names (specialty items): \$9,915,589

Outdoor: 1,474,121

Total: \$11,389,710

**Strategic Goal 2:
Inform and enlist the support of our stakeholders (for example, retailers) and the public to assist in reducing young people's use of and demand for tobacco products.**

Resources: \$22,000,000 6 FTEs

Performance Goals:

- Maintain the percentage of known retailers of cigarettes and smokeless tobacco products who are aware of the FDA tobacco rule at no less than 90 percent and increase the percentage of retailers who understand the age and ID provisions of the rule to 50 percent.
- Promote the availability of free FDA retailer information kits, used to remind customers and young people about the requirements of the FDA tobacco rule, to at least 400,000 retailers of cigarettes and smokeless tobacco products and provide kits to those who request them.

Rationale:

A strong outreach program is one of the most effective ways to increase awareness of and compliance with FDA's restrictions. Currently, the rule requires retailers to check photo identification of every customer under the age of 27 to ensure that no cigarettes or smokeless tobacco products are sold to anyone under the age of 18. Eventually, retailers who operate stores that are accessible to individuals under the age of 18 will have to remove all products from self-service displays and vending machines and relocate them to an area under the retailers control, and to remove illegal advertising. In most cases, retailers will not know all the details of the restrictions that have been placed upon their sale of tobacco. To make it easier for the retailer to understand the new restrictions as well as to enhance compliance with the rules, outreach efforts should be as comprehensive as possible. Moreover, the materials and efforts made to reach retailers should be as useful and informative as possible.

Approaches, Skills, Technology, and External Factors:

FDA uses a multitude of media and approaches to ensure the greatest reach and utility of its messages. FDA maintains a toll free hot line and an Internet site, which permit easy access to answers for frequently asked questions; brochures; and materials. Stores are mailed retailer kits, which include explanations of the requirements, and posters and materials which help explain the rules to customers and assist in defusing customer anger or anxiety. In addition, advertising is placed on radio, in newspapers, and on billboards reminding retailers of their responsibility. These materials are regularly updated and mailed to new retailers or retailers who request the information. In FY 1999, FDA will develop and launch a revised retailer campaign which will build on the increases in retailer knowledge and awareness achieved during 1998. In FY 2000, FDA will continue to update and modestly expand its outreach activities to achieve greater coverage.

FDA is conducting a national advertising campaign aimed at raising retailers' awareness of the new regulations and motivating them to comply. The campaign's primary target audience is managers and clerks in stores that sell tobacco. The campaign was first introduced in FY 1998 in one media market in one state for a four-week period. A survey was conducted in two markets each in ten states (one treatment and one control) to assess the effect of the media campaign in raising retailer awareness of and compliance with the regulations. A total of 2000 managers and clerks were surveyed immediately prior to the campaign and another 2000 were surveyed after the campaign. The data have been collected and are analyzed. FDA intends to continue measuring the effectiveness of its outreach efforts in this manner and to compare results over time.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Maintain the percentage of known retailers of cigarettes and smokeless tobacco products who are aware of the FDA tobacco rule at no less than 90 percent and increase the percentage of retailers who understand the age and ID provisions of the rule to 50 percent.

Data Sources: FDA sponsored surveys of known retailers of cigarettes and smokeless tobacco products to determine awareness and attitude changes.

Baseline Data: A survey was tested in two markets each in ten states in FY 1998. The results are analyzed and will be used to develop baseline data. Based on this limited survey of retailers:

- 97% were aware of the FDA tobacco rule.
- 84% were aware that the legal age for purchase is 18.
- 31-34% were aware that they had to check the ID of every customer under the age of 27.

Goal Statement: Promote availability of free FDA retailer information kits, used to remind customers and young people about the requirements of the FDA tobacco rule, to at least 400,000 retailers of cigarettes and smokeless tobacco products and provide kits to those who request them.

Data Sources: FDA tobacco database

Baseline Data: In FY 1998, approximately 400,000 retailer kits had been mailed.

Strategic Goal 3:

Utilize FDA's regulatory framework to establish and implement a procedure for reviewing existing and new tobacco products to determine the health consequences of specific products or their ingredients, additives or constituents.

Resources: \$4,000,000 5 FTEs

Performance Goal:

- To the fullest extent permitted under any court order, establish the scientific and regulatory framework to address the challenges posed by new and novel nicotine-containing tobacco products as well as issues raised by current products and replacement therapies.

Rationale:

FDA is regulating cigarettes and smokeless tobacco products under the restricted medical device provisions of the Food, Drug and Cosmetic Act (FD&C Act). The FD&C Act requires that all medical devices be classified according to the level of controls necessary to provide reasonable assurance that the product will be safe and effective (see Section 513 of the FD&C Act). Depending upon the classification adopted for tobacco products, it may be appropriate for the Agency to develop performance standards which could include provisions regarding the construction, components and ingredients, and properties of the device and provisions for the testing of the device. All devices are also subject to the requirement that they conform to quality system regulations pursuant to 21 CFR, Part 820. The application of the Act's requirements to tobacco is essential to ensure that the health consequences of products or their ingredients, additives or constituents are made less harmful in order to reduce the death and disease caused by tobacco use.

Approaches, Skills, Technology, and External Factors:

In FY 1999, FDA will begin to address the immediate issues posed by new products and nicotine replacement therapies. In addition, the Agency may begin exploring the questions associated with product regulation including questions raised by classification and quality system regulations. In FY 2000, the Agency will continue the establishment of a regulatory framework necessary to properly analyze the issues related to current and new products. Specifically, it will consider convening an interdisciplinary panel from sister agencies within DHHS including, but not limited to, the National Cancer Institute, the National Heart, Lung and Blood Institute, the Office on Smoking and Health and the National Institute on Drug Abuse to consider and propose appropriate performance standards.

FDA will conduct systematic reviews and evaluations of new and established products that state or imply that they are less harmful.

In FY 2000, the Agency will begin to examine the inspection process by reviewing the practices of the tobacco companies and will continue to assist them in coming into compliance with quality system regulations.

In FY 2000, the Agency will use internal and outside experts, including personnel from sister agencies within DHHS, to begin a review and analysis of ingredients, constituents, and additives.

Performance Goals, Data Sources, and Baselines:

Goal Statement: To the fullest extent permitted under any court order, establish the scientific and regulatory framework to address the challenges posed by new and novel nicotine-containing tobacco products as well as issues raised by current products and replacement therapies.

Data Sources: Internal Agency documents will substantiate progress made.

Baseline Data: These programs have yet to be established and therefore the baseline is zero.

Verification and Validation:

FDA is enforcing the restrictions on youth access that are currently in effect by training and commissioning state regulatory officials, who conduct unannounced purchase attempts using young people under the age of 18 to determine if retailers will sell to minors. The results of each attempt are faxed or mailed to FDA by the state officials. FDA has established a computerized Tobacco database to gather these results, prepare follow-up compliance check forms, send notification of the results to the retailer and ultimately, if necessary, to prepare documents to seek civil money penalties. The database will contain an inventory of retailers of cigarettes and smokeless tobacco products as they are identified. The database allows FDA to track the number of compliance checks, the number of violations (total and broken down by type of store, state, etc.), the number of civil money penalty actions, etc. The data will permit FDA to measure the progress of its enforcement program. However, the data is not statistically projectable, because it is not based on a random sampling of retailers.

In addition, a survey was conducted in two markets each in ten states (one treatment and one control) to assess the effect of the media campaign on raising retailer awareness of and compliance with the regulations. A total of 2000 managers and clerks were surveyed immediately prior to the campaign and another 2000 were surveyed after the campaign. The data have been collected and are analyzed. FDA intends to continue measuring the effectiveness of its outreach efforts in this manner and to compare results over time.

The Federal Trade Commission (FTC) collects and publishes industry-wide data on advertising expenditures by category (e.g., newspapers, outdoor advertising, specialty items). FDA intends to establish the baseline for its advertising goal from FTC data indicating levels of expenditures for each category for the base year, and measuring decreases in spending for each subsequent year. Although this data source cannot measure all of the changes required by the rule (conversion of advertising in publications to black and white text only), it should be able to document whether expenditures for banned advertising (e.g. hats and tee shirts with logos) has ceased and whether declines in expenditures are observed for heavily restricted advertising (e.g. outdoor advertising is banned within 1000 feet of schools and playgrounds and is otherwise restricted to black and white text only format). In addition, the Agency will discuss with FTC the possibility

of including additional questions in their survey of company advertising expenditures to help us more accurately measure compliance with our rule.

FDA's tobacco program is not fully in effect. A court order has stayed implementation of most of the regulation. Until other parts of the rule are in effect, more elaborate measurement cannot begin. FDA is working closely with CDC's Office on Smoking and Health, SAMHSA and the Data Council of DHHS to devise and conduct surveys to measure success in reducing initiation and use of tobacco by young people. The Agency is also monitoring compliance with the rule, assessing buy rates, determining reach and effect of outreach efforts, and assessing the risks of various components of tobacco products to determine whether it is possible to reduce the overall health risks associated with tobacco products. One of the first responsibilities of the Tobacco Program following lifting of the court stay or enactment of comprehensive legislation, will be to devise and implement a surveillance mechanism to establish bench mark levels for these goals including but not limited to youth tobacco initiation and use rates and risk levels of current products and ingredients. This surveillance effort will enable the Agency to validly measure progress.

Disposition of FY 1999 Goals

Last Revised: January 1999

Note: This list excludes FY 1999 goals added after January 1998. For a complete list of FY 1999 goals see [Appendix 2: FY 1999 and FY 2000 FDA Performance Plan Summary](#)

	<u>Original Goal Statement¹</u>	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
Foods				
11001	By the end of FY 1999, complete reviews of 30% of food and color additive petitions within 360 days.	Revised	Complete first action (i.e., review all parts of the petition and issue a "not approvable" letter, or publish a response in the Federal Register, if appropriate) on 30 percent of food and color additive petitions within 360 days of receipt.	Revised to be consistent with FY2000 performance goal on petition reviews.

11002	By the end of FY 1999, reduce the number of overdue food and color additive petitions to 30% of those petitions under review.	Revised	By the end of FY 1999, reduce the percentage of overdue food and color additive petitions (i.e., under review for more than 360 days) to 30 percent of those petitions under review.	Revised to be consistent with FY2000 performance goal.
11003	During FY 1999, finalize the rulemaking creating a premarket notification process for independent generally recognized as safe (GRAS) determinations.	Unchanged		
11004	By 12/30/99, 50% of the seafood industry will be operating preventive controls for safety as evidenced by functioning, appropriate HACCP systems.	Revised	By 12/30/99, 50% of the domestic seafood industry will be operating preventive controls for safety as evidenced by functioning HACCP systems.	Revised to be consistent with FY2000 performance goal.
11005	Increase the percentage of domestic produce produced consistent with voluntary good agricultural practices (GAP)/good manufacturing practices (GMP) broadscope guidance to reduce microbial contamination.	Unchanged		
11006	During FY 1999, take steps to implement the HACCP regulation for the juice industry, including providing	Revised	During FY 1999, develop HACCP final rule for fruit and vegetable juices.	Change in FY 1999 Appropriation level from funding

	training, technical assistance and guidance to industry and states.			levels in President's Budget.
11007	By the end of FY 1999, increase to at least 77% the proportion of people aged 18 and over who use food labels to make nutritious food selections.	Unchanged		
11008	During FY 1999, work with the Centers for Disease Control and Prevention (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.	Unchanged		
11009	By the end of FY 1999, improve public access to timely information on adverse events related to dietary supplement products, infant formulas, and medical foods by increasing the frequency of public releases of information in the Special Nutritional Adverse Events Monitoring System (SN/AEMS) from 2 per year to 4 per year.	Unchanged		
11010	By the end of FY 1999, enhance the safety of the nation's food supply by achieving adoption of the	Unchanged		

	Food Code by 25% of the states.			
11011	Assure that FDA inspections of domestic food manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements by the end of the fiscal year.	Unchanged		
11012	Implement a multi-year research plan to develop and improve methods for the detection, control and prevention of microbial contamination on fresh produce and evaluate the effectiveness of technologies for eliminating this contamination.	Unchanged		
11013	During FY 1999, develop modeling techniques for assessing human exposure to a variety of foodborne pathogens and for describing low dose infectivity rates for infectious and toxicoinfectious microorganisms.	Unchanged		
11014	During FY 1999, work with industry and academia to develop new techniques for eliminating pathogens on fresh produce where	Revised	During FY 1999, work with industry and academia to develop new techniques for eliminating	Change in FY 1999 Appropriation from funding levels in President's

	traditional thermal processing systems used for processed foods cause fresh produce to deteriorate and become inedible.		pathogens on sprouts and in citrus juice and apple cider.	Budget.
11015	During FY 1999, conduct studies on factors that cause foodborne pathogens to develop multiple antibiotic resistance and resistance to traditional food preservation techniques and factors that prevent the development of such resistance.	Unchanged		
11016	Use educational campaigns and activities to reduce the prevalence of reported risky food consumption behavior, reduce the prevalence of reported risky food preparation/handling practices, and increase the percentage of people who report using thermometers to assure the safety of foods during cooking.	Revised	Use educational campaigns and activities to reduce the prevalence of reported risky food consumption behavior, reduce the prevalence of reported risky food preparation/handling practices, and document the occurrence of food service behaviors, actions, and conditions that fall into the CDC-identified risk factor categories classified as "contributing factors to foodborne illness outbreaks."	Restated to more clearly express the focus of the goal.
11017	During FY 1999, increase the safety of imported foods through participation in	Revised	During FY 1999, increase the safety of imported foods through	Change in FY 1999 appropriation from funding

	<p>international standard setting organizations (such as Codex Alimentarius of the United Nations World Health Organization (WHO) and the Food and Agricultural Organization (FAO), the North American Free Trade Agreement's (NAFTA) Standard Phytosanitary Committee, and the World Trade Organization (WTO)) that consider or establish international standards for food safety and sanitation.</p>		<p>participation in international standard setting organizations and the negotiations of the free trade agreement of the Americas to ensure and international food safety standards are science-based and properly used.</p>	<p>levels in the President's Budget.</p>
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Human Drugs

	<p><u>Original Goal Statement</u>¹</p>	<p><u>Disposition</u></p>	<p><u>Revised Goal</u></p>	<p><u>Explanation</u></p>
<p>12002</p>	<p>Review and act on 90% of complete NDA applications resubmitted following receipt of a non-approval letter, within six months after resubmission date.</p>	<p>Unchanged</p>		
<p>12003</p>	<p>Review and act upon 60% of fileable original generic drug applications within six months after submission date.</p>	<p>Unchanged</p>		
<p>12004</p>	<p>Review and act upon 90% of standard efficacy supplements within 12 months (30% within 10 months of receipt) and priority efficacy supplements filed within</p>	<p>Unchanged</p>		

	six months of receipt.			
12005	Review and act upon 90% of manufacturing supplements within six months and act on 30% of manufacturing supplements requiring prior approval within four months.	Unchanged		
12006	Assure the FDA inspections of domestic drug manufacturing and repackaging establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements by the end of the fiscal year.	Unchanged		
12007	Implement the Adverse Events Reporting System (AERS) for the electronic receipt and review of voluntary and mandatory ADE reports.	Unchanged		
12008	Establish the capability and capacity to receive and archive Abbreviated New Drug Applications (ANDAs) submitted electronically.	Revised	Continue to achieve capability and capacity for electronic submission and archiving of information required to submit new drug applications (NDAs), abbreviated new drug applications (ANDAs)	Regarding Abbreviated Antibiotic Drug Applications (AADAs), FDAMA eliminated the AADAs as a separate submission type. All existing AADAs were

				converted to Drug Master Files (DMF) and future submissions will come in as DMFs. DMFs are planned for electronic receipt, storage, and archive by the end of FY 2002.
12009	FDA will: (a) evaluate the availability, quality and usefulness of prescription drug information provided to 75% of individuals receiving new prescriptions; and (b) complete two studies that will aid in development of comprehensive drug information.	Unchanged		
12010	FDA will continue to improve the legibility and clarity of OTC drug labels, and improve the consumer's ability to read and understand important warnings and usage directions.	Unchanged		
Biologics				
	<u>Original Goal Statement</u> ¹	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
13001	Review and act on 90% of standard New Drug Applications (NDA) and	Unchanged		

	<p>Product License Applications/ Biologics License Applications (PLA/BLA) filed within 12 months after receipt (30% within 10 months of receipt); and review and act on 90% of priority NDA and PLA/BLA submissions within six months of receipt.</p>			
13002	<p>Review and act on 90% of standard efficacy supplements within 12 months of receipt (30% within 10 months of receipt); and review and act on 90% of priority efficacy supplements within six months of receipt.</p>	Unchanged		
13003	<p>Review and act on 90% of manufacturing supplements filed within six months of receipt, and review and act on 30% of manufacturing supplements requiring prior approval within four months of receipt.</p>	Unchanged		
13004	<p>Review and act on 90% of Class 1 resubmitted original applications within four months of receipt (50% within two months of receipt); and review and act on 90% of Class 2 resubmitted original applications within six months of receipt.</p>	Unchanged		

13005	Review and act on 70% of complete blood bank and source plasma PLA/BLA submissions and PLA/BLA Major supplements within 12 months after submission date.	Revised	Review and act on 60% of complete blood bank and source plasma PLA/BLA submissions and 90% of PLA/BLA Major supplements within 12 months after submission date.	Revised to be consistent with FY2000 performance goal; diversion of resources required and resource cuts in FY99.
13006	Review and act on 60% of complete blood bank/source plasma Establishment License Applications (ELA) Major supplements within 12 months after submission date.	Dropped		Establishment License Applications (ELAs) and ELA supplements are being phased out with the adoption of the Biologics License Application (BLA), which will replace the Product License Application (PLA) and ELA. The Goal was not included in the FY 2000 plan.
13007	Assure that FDA inspections of domestic biologics manufacturers and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these	Unchanged		

	inspections, result in a high rate of conformance (at least 90%) with FDA requirements by the end of the fiscal year.			
13008	Increase the percentage of plasma fractionator establishments in compliance with current good manufacturing practices (CGMPs) to 80 percent.	Revised	Increase the percentage of plasma fractionator Establishments in compliance with Current Good Manufacturing Practices (CGMPs) to 70 percent.	FY 1997 and FY 1998 actual performance lower: change in FY 1999 and in subsequent target levels

Animal Drugs and Feeds

	<u>Original Goal Statement¹</u>	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
14001	Improve application processing by implementing ADAA legislation and CVM REGO initiatives, including the Veterinary Feed Directive (VFD), by establishing and/or revising regulations and guidance documents.	Unchanged		
14002	Improve application processing time by implementing electronic submission for key components of the investigational new animal drug application process.	Unchanged		
14003	Increase the number of antimicrobial product risk assessments by 10% in order to increase the assurance that food	Unchanged		

	derived from animals and animal products is safe for human consumption.			
14004	Assure that FDA inspections of domestic animal drug and feed manufacturing establishments, in conjunction with the timely corrections of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90%) with FDA requirements by the end of the fiscal year.	Unchanged		
14005	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 National Antimicrobial Monitoring Program database.	Revised	Maintain the bacterial isolate testing rate from human and animal origin in the National Antimicrobial Resistance Monitoring System (NARMS) database at 2,000 and 4,000 respectively	More specific targets
14006	Protect public health (human) and animal health by ensuring compliance with good manufacturing practices including the newly implemented BSE (Mad Cow Disease) regulation through education, regulatory inspections and industry/Federal/state partnerships.	Unchanged		

Medical Devices and Radiological Health

	<u>Original Goal Statement¹</u>	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
15001	Complete 50% of PMA first actions within 180 days.	Revised	Maintain the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first actions (within 75 days) completed at 65 percent.	Better baseline data; funding change
15002	Complete 90% of 510(k) first actions within 90 days. Expand third party 510(k) reviews and complete FDA action on 55% of them within 30 days.	Revised	Review and complete 90 percent of 510(k) first actions within 90 days. Expand third party 510(k) reviews and complete FDA action on 75% of them within 30 days.	Better baseline data
15003	Recognize over 50 standards for use in application review and update the list of recognized standards.	Revised	Recognize over 415 standards for use in application review and update the list of recognized standards.	Better baseline data
15004	Double the number of low-risk postmarket reports received and processed in summary form. The total number of summary reports will be increased from 25,000 in FY 1998 to over 60,000 in FY 1999. This will be done by shifting postmarket reporting from a paper-intensive	Revised	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 1998 to over 25,000 in FY 1999. This	Funding reduced

	individual report system (receiving over 100,000 reports in FY 1996) to an alternate almost entirely electronic reporting system, yielding higher quality information using innovative surveillance methodology like auto screen and developing variances candidates.		will be done using innovative surveillance methods and improving quality and analysis needed for Safety Alerts and other actions.	
15005.01	Improve the quality conformance of high-risk products like cardiovascular devices by redirecting FDA compliance priorities toward higher-risk devices.	Revised	Improve the quality conformance of high-risk products like cardiovascular devices by committing over 75% of inspection resources to high-risk devices.	Goal focused to measure specific resource investment.
15007	At least 97% of mammography centers meet key inspection standards, with less than 3% of facilities with Level I (serious) inspection problems.	Revised	Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level I (serious) inspection problems.	Minor editorial changes.
15008	Improve response to significant risk electronic product radiation noncompliance by initiating regulatory actions and recalls for 95% of identified high-risk noncompliant or defective products within 30 days of discovery.	Revised	Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95 percent of identified high-risk, noncompliant or defective products within 30 days of discovery.	Minor editorial changes.

15018	Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 95%) with FDA requirements by the end of the fiscal year.	Revised	Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements.	Reduced funding required lowering target level.
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National Center for Toxicological Research

	<u>Original Goal Statement¹</u>	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
16001	Demonstrate a model toxicity knowledge base to support and expedite product review.	Unchanged		
16002	Develop better biological assays to measure genetic changes and predict human genetic damage.	Unchanged		
16003	Complete biochemical and epidemiology studies to define the basis of susceptibility of humans to the toxicity of regulated products.	Unchanged		
16004	Develop modeling tools to predict better risk for cancer, reproductive, developmental, neurological, genetic, and acute toxicological outcomes.	Unchanged		

16005	Support product review by developing faster, more accurate tests based on mechanisms of toxic actions.	Unchanged		
16006	Develop rapid and sensitive methods for identifying pathogens, foodborne bacteria, and microbial contaminants.	Unchanged		
Tobacco				
	<u>Original Goal Statement</u>¹	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
17001	Enter into contracts with all 50 states (depending on their willingness) to conduct an average of 42,000 unannounced compliance checks each month of retail establishments that sell tobacco products. each month of retail establishments that sell tobacco products.	Revised	Enter into contracts with all 50 states (or establish a federal investigatory force in those states which are unable or unwilling to contract with FDA), to conduct an average of 16,500 unannounced compliance checks	Funding level reduced.
17002	Conduct meetings and a multimedia campaign, including point-of-purchase, radio, outdoor advertising, and newspapers, to educate retailers and other stakeholders about their obligations under the FDA tobacco rules and the impact of the rules. Distribute at least 100,000 brochures and fact sheets to retailers on request.	Revised	Conduct meetings and a multimedia campaign, including point-of-purchase, radio, outdoor advertising, and newspapers, to educate retailers and other stakeholders about their obligations under the FDA tobacco rules and the impact of the rules.	Funding level reduced; scope of goal reduced accordingly.

17003	<p>Design and, to the fullest extent permitted under any court orders addressing such activities, begin to implement a regulatory program for cigarettes and smokeless tobacco products, including:</p> <ul style="list-style-type: none"> - Begin to examine the appropriate scientific and regulatory framework to evaluate products that state or imply that they are less hazardous; - Assist other agencies within the Department of Health and Human Services in providing the Federal Trade Commission with an analysis of the public health issues associated with the testing and reporting of the tar and nicotine content of the smoke of cigarettes; and - Establish an evaluation and review procedure for new products. 	Dropped		No funding.
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Imports

	<u>Original Goal Statement</u> ¹	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>
18001	Accept at least 20% of imports into the U.S. market through evidence of equivalent source country quality systems/standards/audits.	Dropped		International trade agreements with foreign nations are at various stages of development. Definitions of 'equivalence'

				must first be determined before baseline data for this goal can be developed.
18002	Enhance import screening capabilities for public health while ensuring that 55% of entries are released within 15 minutes.	Revised	Complete design specifications for an analysis that is efficiency to a determination of risk-based screening criteria for import entries.	Strategy has shifted from measures of system intended to profile variations in criteria used by different FDA programs in screening import entries.
18003	Assess potentially violative imports through direct examination of 3% of entries.	Dropped		Strategic emphasis has shifted to prevent activities at the source of production and development of risk. Small percentages of potentially high-risk products will still be directly examined.
External Leverage				
	<u>Original Goal Statement¹</u>	<u>Disposition</u>	<u>Revised Goal</u>	<u>Explanation</u>

19001	Expand the system of State Partnership Agreements to comprise at least one per state to increase both quality and efficiency between the Federal, state, and local officials.	Dropped		Not outcome-oriented
19002	Publicize and conduct 75 workshops for regulated industry coordinated and/or sponsored by the FDA field offices focusing on providing Agency-wide product line training that results in increased compliance and consumer protection.	Dropped		Not outcome-oriented
19003	Correct a majority of significant problems identified in manufacturing/processing operations via prompt, cooperative action.	Dropped		Not outcome oriented; concept included in program conformance goals

1. As shown in FY 1999 Congressional Justification

FY 1999 and FY 2000 FDA Performance Plan Summary

(Last Revised: 9/8/1999)

[Foods](#) | [Human Drugs](#) | [Biologics](#) | [Animal Drugs and Feeds](#)
[Medical Devices and Radiological Health](#) | [National Center for Toxicological Research](#)
[Tobacco](#) | [Imports](#)

Note: Italicized goal statements appearing in the FY 1999 performance goal column are not contract goal commitments for FY 1999, but are provided as baselines for FY 2000 performance goals.

	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Foods	FY 1998 Actual: \$206,249.00	FY 1999 Current: \$231,580.00	FY 2000 Request: \$275,955.00
11001	Developed and tested an electronic workflow system that will facilitate tracking and assignment of petition reviews. Additional work required to make the system fully operational by the end of FY 1999 was not funded in FY 1998.	Complete first action (i.e., review all parts of the petition and issue a "not approvable" letter, or publish a response in the Federal Register, if appropriate) on 30 percent of food and color additive petitions within 360 days of receipt. 1,3 <i>The workflow system will be operational (target)</i>	Complete first action (i.e., review all parts of the petition and issue a "not approvable" letter, or publish a response in the Federal Register, if appropriate) on 40 percent of food and color additive petitions within 360 days of receipt. 3
11002	38%. Develop electronic workflow system to facilitate tracking and assignment of petition reviews (target).	By the end of FY 1999, reduce the percentage of overdue food and color additive petitions (i.e., under review for more than 360 days) to 30 percent of those petitions under review.	Reduce the percentage of overdue food and color additive petitions (i.e., under review for more than 360 days) to 20 percent of petitions under review.
11003	Under development. FDA currently does not have quantitative data to establish a baseline for this goal. Baseline data are expected for FY 1999. The projected goal is based on the FDA's analysis of its experience thus far implementing this process on an interim basis.	During FY 1999, finalize the rulemaking creating a premarket notification process for independent generally recognized as safe (GRAS) determinations. 3	Complete processing of 80 percent of generally recognized as safe (GRAS) notifications within the time frame established by the final rule. 3
11004	Conducted 3,876 initial HACCP verification inspections.	By 12/30/99, 50 percent of the domestic seafood industry will be operating preventive	Eighty percent of the domestic seafood industry will be operating preventive

		controls for safety as evidenced by functioning Hazard Analysis and Critical Control Point (HACCP) systems. 1	controls for safety as evidenced by functioning Hazard Analysis and Critical Control Point (HACCP) systems.
11005	Conducted grassroots meetings on GAP and GMP guidance with domestic and foreign fresh produce growers, producers, processors and manufacturers. Issued broad-scope guidance on GAPs/GMPs for growers and producers of fruits and processors of fresh produce.	Increase the percentage of domestic produce produced consistent with voluntary good agricultural practices (GAP)/good manufacturing practices (GMP) broadscope guidance to reduce microbial contamination. 3 <i>Complete a pretest of the survey instrument by early FY 1999. Assuming OMB approval under the Paperwork Reduction Act, surveys will be conducted in New York State and California covering 20 of the of the most-consumed fruits and vegetables.</i>	Continue to develop and implement voluntary guidance and other efforts to improve the safety of fresh fruits and vegetables, and work with USDA to conduct a 1999-2001 National Agricultural Statistics Survey (NASS) of microbial contamination of fresh produce to collect the data required to evaluate program effectiveness. 3
11006	Published a proposed regulation for juice HACCP and evaluated comments.	During FY 1999, develop the Hazard Analysis and Critical Control Point (HACCP) final rule for fruit and vegetable juices. 3	Initiate Hazard Analysis and Critical Control Points (HACCP) systems in the juice industry. 3
11007		By the end of FY 1999, increase to at least 77% the proportion of people aged 18 and over who use food labels to make nutritious food selections.	Increase to at least 55 percent the proportion of adults who report changing their decision to buy or use a food product because they read the food label.
11008	Expanded the demographic diversity	During FY 1999, work with the Centers for	Work with the Centers for Disease Control and

	and size of the population covered by FoodNet by increasing the number of active surveillance sites from 7 to 8. Began implementation of PulseNet which provides data required to do more rapid and accurate tracebacks to determine the causes of foodborne illness outbreaks.	Disease Control and Prevention (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. 1 <i>Continue FoodNet and add more states to PulseNet.</i>	Prevention (CDC), the U.S. Department of Agriculture (USDA), and states to increase food safety surveillance and to improve responses to foodborne illness outbreaks.
11009		By the end of FY 1999, improve public access to timely information on adverse events related to dietary supplement products, infant formulas, and medical foods by increasing the frequency of public releases of information in the Special Nutritional Adverse Events Monitoring System (SN/AEMS) from 2 per year to 4 per year. 1 <i>The requisite hardware and software systems need to be purchased for integration of current Center-based systems with limited capacity.</i>	Establish an integrated adverse event reporting system for food and cosmetic products, with emphasis on increasing efforts to design and implement modules needed to record dietary supplement adverse event information.
11010	Ten states/jurisdictions (20%) reported adopting the Food Code.	By the end of FY 1999, enhance the safety of the nation's food supply by achieving adoption	Achieve adoption of the Food Code by at least 35 percent of the states.

		of the Food Code by 25 percent of the states.	
11011	98%	Assure that FDA inspections of domestic food manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements by the end of the fiscal year. 3	Assure that FDA inspections of domestic food establishments (excludes domestic seafood establishments), in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements. 3
11012	Developed and began implementing an interagency research plan that more effectively coordinates the food safety research activities in FDA and USDA.	Implement a multi-year research plan to develop and improve methods for the detection, control and prevention of microbial contamination on fresh produce and evaluate the effectiveness of technologies for eliminating this contamination. 1	Develop and make available an improved method for the detection of hepatitis A virus, Cyclospora cayetanensis and Escherichia coli O157:H7 on additional fruits and vegetables, and provide knowledge and technologies needed to develop guidance and methods for the control and elimination of pathogens on particular fruits and vegetables such as Escherichia coli O157:H7 and Salmonella spp. from juices, leafy vegetables and sprouted seeds and Cyclospora from soft fruit (e.g., berries).
11013		During FY 1999, develop modeling techniques for assessing human exposure to a	Develop modeling techniques to assess human exposure and dose-response to certain

		variety of foodborne pathogens and for describing low dose infectivity rates for infectious and toxicoinfectious microorganisms. 1, 3	foodborne pathogens, the potential risk for those pathogens causing human illness, and the setting of safety performance standards to regulate microbial content of food towards reducing incidence of foodborne disease.
11014		During FY 1999, work with industry and academia to develop new techniques for eliminating pathogens on sprouts and in citrus juice and apple cider. 1	
11015	These phenomena are recent developments and very little research has been conducted to date. The FY 1999 studies will fill this gap.	During FY 1999, conduct studies on factors that cause foodborne pathogens to develop multiple antibiotic resistance and resistance to traditional food preservation techniques and factors that prevent the development of such resistance.	
11016	Continue developing data collection instrument for FDA's FY 1998 Consumer Survey; Collect data for FDA's FY 1998 Consumer Survey; Develop and launch educational campaigns and activities on risky food consumption behavior targeting special populations for key safety messages, promoting the use of the Food Code and	Use educational campaigns and activities to reduce the prevalence of reported risky food consumption behavior, reduce the prevalence of reported risky food preparation/handling practices, and document the occurrence of food service behaviors, actions, and conditions that fall into the CDC-identified risk factor categories classified as	

	science-based safety standards, and overcoming barriers to communicating proper food safety behaviors to food service workers.	"contributing factors to foodborne illness outbreaks."	
11017		During FY 1999, increase the safety of imported foods through participation in international standard setting organizations and the regulations of the free trade agreement of the Americas to ensure that international food safety standards are science-based and properly used.	
11018		<i>Under development. Baseline data are expected for FY 1999.</i>	Complete initial processing of 80 percent of biotechnology consultations within established time frames. 3
11019	Received and processed three health claims.	<i>Receive and process three health claims.</i>	Respond to 95 percent of nutrient content claim and health claim petitions/notifications within the statutory and regulatory time frames.
11020	Through a combination of FDA and state contract inspections, cover 25% to 33% of the 6,250 high risk food establishments.	<i>Through a combination of FDA and state contract inspections, cover 25 percent to 33 percent of the 6,250 high risk food establishments.</i>	Increase the frequency of high-risk domestic food establishment inspections to once every one to two years, and annually beginning in FY 2001.
11021.01	Conducted 43 foreign inspection/evaluations.	During FY 1999, enhance the safety of imported products through surveillance of imported food products	Increase the number of inspections/ evaluations of foreign food establishments from 100 to 250.

		at the border, increase foreign inspections (from 40 to 75-100), provide education, outreach and evaluate food production systems in foreign countries. 1	
11022		<i>Baseline data do not currently exist for these research activities.</i>	Develop more rapid and accurate analytical methods for foodborne chemical contaminants (including bacterial toxins).
11023		<i>FDA suspended operation of the cosmetic voluntary reporting program in March 1998 due to budget shortfalls. The database has been maintained since it was suspended but has not been updated with any new submissions. In FY1999, the Agency will work with the regulated industry to update the database for voluntary reporting. The updated database will provide the information required to establish an accurate baseline for this activity.</i>	Maintain the restored level of activity for cosmetic voluntary reporting to protect consumers against potentially hazardous cosmetic ingredients or products.
11024		<i>Systems to collect data to establish baselines are under development and will be implemented when the program for food contact substances is developed and becomes operational.</i>	Finalize guidance and regulations necessary to support operations of the premarket notification program for food contact substances established by FDAMA and as set out in Sec. 409(h) of the FD&C

			Act. 3
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Human Drugs	FY 1998 Actual: \$262,648.00	FY 1999 Current: \$291,981.00	FY 2000 Request: \$316,760.00
12001	100% of those acted on (some pending, not overdue)	Review and act on 90 percent of standard new drug applications (NDAs) filed within 12 months after receipt (30 percent within 10 months of receipt); and 90 percent of priority applications within six months.	Review and act on 90 percent of standard original New Drug Application (NDA) submissions within 12 months of receipt (50 percent within 10 months); and 90 percent of priority original NDA submissions within 6 months.
12002		Review and act on 90 percent of complete NDA applications resubmitted following receipt of a non-approval letter, within six months after resubmission date.	
12003		Review and act upon 60 percent of fileable original generic drug applications within six months after submission date. 1	
12004	100% of those acted on (some pending, not overdue).	Review and act upon 90 percent of standard efficacy supplements within 12 months (30 percent within 10 months of receipt) and priority efficacy supplements filed within six months of receipt. 1	Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and 90 percent of priority efficacy supplements within 6 months of receipt.
12005		Review and act upon 90 percent of manufacturing supplements within six	

		months and act on 30 percent of manufacturing supplements requiring prior approval within four months.	
12006	93%	Assure that FDA inspections of domestic drug manufacturing and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements by the end of the fiscal year. 3	Assure that FDA inspections of domestic drug manufacturing and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements by the end of the fiscal year. 3
12007	Pilot, five firms electronic entry, uncoded only. Periodic reports only.	Implement the Adverse Events Reporting System (AERS) for the electronic receipt and review of voluntary and mandatory ADE reports. 1 <i>50% of top 15 drug companies electronically submitted, half of that group coded using International Conference on Harmonization (ICH) Medical Dictionary for Regulatory Activities (MedDRA) terminology, begin expedited report entry.</i>	Expedite processing and evaluation of adverse drug events through implementation of the Adverse Events Reporting System (AERS) which allows for electronic periodic data entry and acquisition of fully coded information from drug companies.
12008	Public comments on the industry guidance for the full NDA are	Continue to achieve capability and capacity for Electronic	Establish the capability and capacity to receive and archive abbreviated

	resolved.	<p>submission and archiving of information required to submit new drug applications (NDAs) and abbreviated new drug applications (ANDAs).</p> <p><i>All NDAs submitted electronically can be received and archived; industry guidance for electronic ANDAs is published for public comment; a pilot is conducted with up to 25 ANDAs submitted electronically.</i></p>	new drug applications (ANDAs) submitted electronically.
12009	Initiate studies to evaluate usefulness of information received by patients who are receiving new prescriptions.	FDA will: (a) evaluate the availability, quality and usefulness of prescription drug information provided to 75% of individuals receiving new prescriptions; and (b) complete two studies that will aid in development of comprehensive drug information. 1	
12010	A proposal providing for standardized format for labeling was published in the <i>Federal Register</i> on 2/27/98. Study topics were identified and studies were designed.	FDA will continue to improve the legibility and clarity of OTC drug labels, and improve the consumer's ability to read and understand important warnings and usage directions. 1	
12011		<i>To be established 10/1/99. Parameters will be established for the new reports which show performance</i>	Provide written responses to industry within 14 days of receipt on 80 percent of formal meeting

		<p><i>relating to PDUFA goals and provide necessary day-to-day management of the process. The reports will be in place by the end of the first quarter of FY 1999. 3</i></p>	<p>requests; make meeting minutes available to sponsors within 30 calendar days for 80 percent of meetings; and, ensure that 80 percent of Type A meetings are scheduled within 30 calendar days of receipt of the meeting request, Type B within 60 calendar days of receipt of meeting request, and Type C meetings within 75 calendar days of receipt of meeting request. 3</p>
12012	<p>(As of March 1998) CDER web site users - 115,273 Number of page hits/accesses - 2,250,574 70% of approval letters posted in 15 days 90% of approval letters posted in 30 days Most reviews not posted Zero new molecular entity (NME) consumer drug information sheets Zero prescribing information sheets</p>	<p><i>All FY 1997 and FY 1998 New Molecular Entities available on the world wide web (target).</i></p>	<p>Make new drug approval information increasingly available and targeted and promoted to specific user groups, such as consumers, patients, health-care practitioners and industry via the Internet, resulting in a decrease in serious medication errors.</p>
12014	<p>Complete initial research and develop guidance for studies <i>in vitro</i>.</p>	<p><i>Complete collaborative studies in vivo to confirm scale up from in vitro and to optimize metabolite: parent ratios.</i></p>	<p>Complete 75 percent of projects identified in CDER's Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) designed to lead to appropriate policy for applying modern <i>in vitro</i> and <i>ex vivo</i></p>

			technology to assess drug metabolism and drug interactions.
12015		<i>Requirements of Section 127 of FDAMA</i>	Develop a list of bulk drug substances that may be used in compounding and publish a rule to be used for pharmacy compounding.
12016	Formalize the PQRI collaboration	<i>Initiate research projects under direction of PQRI and continue to plan and review activities of technical Committees and working groups.</i>	Complete 25 percent of the research projects started in FY 1999 under the auspices of the Product Quality Research Initiative (PQRI), a collaboration among FDA, industry and academia established to provide a scientific basis for policy and guidance development in CDER on issues of drug product quality and performance.
12017	Identify specific issues and areas of research focus and develop research protocols.	<i>Initiate research and apply appropriate technologies to address specific issues including, where necessary, establishing tests and models for accurate evaluation.</i>	Complete 75 percent of research projects identified in the Office of Testing and Research (OTR) Research Plan (dated November 24, 1997) designed to develop rational, scientific-based requirements for drug substances, drug products and excipients to ensure a high standard of drug product quality and product performance for making regulatory decisions.
12018	Formulate evaluation	<i>Establish baseline</i>	Reduce the number per

	<p>plan to establish baseline criteria. Analyze data on wide variability in the number of manufacturing supplements; determine if extraneous factors can be eliminated to establish a stable baseline. Establish what surrogate measures could be used in the absence of a stable baseline.</p>	<p><i>against which a target level of reduced supplements can be set.</i> 3</p>	<p>application of post-approval changes requiring chemistry supplements. 3</p>
12019	<p>Target 25% of review documents processed using EDMS</p>	<p><i>Target 50% of review documents processed using EDMS</i></p>	<p>Process 75 percent of all review documents by implementing an Electronic Document Management System (EDMS) throughout new and generic drug review divisions.</p>
12020	<p>24%</p>	<p>Inspect 22 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers. 1, 2</p>	<p>Improve inspection coverage by inspecting 36 percent of registered human drug manufacturers, repackers, relabelers and medical gas repackers.</p>
12024	<p>114 (estimate)</p>	<p><i>115 (target)</i></p>	<p>Increase the average monthly number of actions (approvals, tentative approvals, not approvals, and facsimile requests) completed on Abbreviated New Drug Applications (ANDAs) by 3.2 percent from the FY 1997 level.</p>
12025	<p>Two national organizations working with CDER as partners</p>	<p><i>Four national organizations working with CDER as partners</i></p>	<p>Develop partnerships with 8 national organizations to</p>

	to develop initiatives and disseminate information	<i>to develop initiatives and disseminate information.</i>	disseminate educational information to consumers about choosing the right medications, taking medications correctly and reporting adverse reactions.
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Biologics	FY 1998 Actual: \$123,012.00	FY 1999 Current \$125,095.00	FY 2000 Request: \$138,114.00
13001	Standard Applications within 12 months: 90% (estimate) ; Standard Applications within 10 months: NA ; Priority Applications within 6 months: 90% (estimate)	Review and act on 90 percent of standard New Drug Applications (NDA) and Product License Applications/Biologics License Applications (PLA/BLA) filed within 12 months after receipt 30 percent within 10 months of receipt); and review and act on 90 percent of priority NDA and PLA/BLA submissions within six months of receipt. <u>1</u>	Review and act on 90 percent of standard original New Drug Application (NDA), Product License Application (PLA) and Biologic License Application (BLA) submissions within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority original NDA/PLA/BLA submissions within 6 months of receipt.
13002	Standard Applications within 12 months: 90% (estimate) Standard Applications within 10 months: NA. Priority Applications within 6 months: 90% (estimate)	Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (30 percent within 10 months of receipt); and review and act on 90 percent of priority efficacy supplements within six months of receipt. <u>1</u>	Review and act on 90 percent of standard efficacy supplements within 12 months of receipt (50 percent within 10 months); and review and act on 90 percent of priority efficacy supplements within 6 months of receipt.
13003	Within 6 months: 90% (estimate) Within 4 months: NA	Review and act on 90 percent of manufacturing supplements filed	Review and act on 90 percent of manufacturing supplements within 6

		within six months of receipt, and review and act on 30 percent of manufacturing supplements requiring prior approval within four months of receipt.	months of receipt, and review and act on 50 percent within 4 months of receipt.
13004	Resubmissions within 6 months: 90% (estimate); Class I resubmissions within 6 months: 90% (estimate); Class I resubmissions within 2 months: 30% estimate); Class I resubmissions within 4 months: NA; Class II resubmissions within 6 months: NA	Review and act on 90 percent of Class 1 resubmitted original applications within four months of receipt (50 percent within two months of receipt); and review and act on 90 percent of Class 2 resubmitted original applications within six months of receipt.	Review and act on 90 percent of Class 1 resubmitted original applications within 4 months of receipt (review 50 percent within 2 months); and review and act on 90 percent of Class 2 resubmitted original applications within 6 months of receipt.
13005	Complete Submissions: 70% (estimate). Major Supplements: 90%(estimate).	Review and act on 60 percent of complete blood bank and source plasma Product License Application (PLA)/Biologic License Application (BLA) submissions and 90 percent of PLA/BLA Major supplements within 12 months after submission date. 1, 2	Review and act on 85 percent of complete blood bank and source plasma Product License Application (PLA)/Biologic License Application (BLA) submissions and 90 percent of PLA/BLA Major supplements within 12 months after submission date.
13007	97%	Assure that FDA inspections of domestic biologics manufacturers and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA	Assure that FDA inspections of domestic biologics manufacturers and repacking establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high conformance rate with FDA requirements (at least 90 percent). 3

		requirements. 3	
13008	13 of 24 plasma fractionator establishments were considered in compliance (54%).	Increase the percentage of plasma fractionator establishments in compliance with Current Good Manufacturing Practices (CGMPs) to 70 percent.	Increase the percentage of plasma fractionator establishments in compliance with Current Good Manufacturing Practices (CGMPs) to 80 percent.
13012	46%	Inspect 43 percent of registered blood banks, source plasma operations and manufacturing establishments. 1,2	Meet the biennial inspection statutory requirement by inspecting 50 percent of registered blood banks, source plasma operations and biologics manufacturing establishments.
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Animal Drugs and Feeds	FY 1998 Actual: \$41,354.00	FY 1999 Current: \$41,973.00	FY 2000 Request: \$52,473.00
14001	Review guidance documents to identify documents for preparation or rewriting.	Improve application processing by implementing ADAA legislation and CVM REGO initiatives, including the Veterinary Feed Directive (VFD), by establishing and/or revising regulations and guidance documents. 1 <i>Update 1% of guidelines (target)</i>	Update 10 percent of the animal drug review guidelines, which serve as aids to industry in the animal drug review process.
14002	Completed pilot to permit electronic submissions of Notices of Claimed Investigational Exemptions (NCIE)	Improve application processing time by implementing electronic submission for key components of the investigational new	Reduce drug development and review time through implementation of additional phases of electronic submission in

		<p>animal drug application process.</p> <p><i>2 phases (target): Drug Shipment Notices, Notices of Slaughter</i></p>	<p>the investigational new animal drug development process.</p>
14003		<p>Increase the number of antimicrobial product risk Assessments by 10% in order to increase the assurance that food derived from animals and animal products is safe for human consumption.</p> <p><i>1 assessment (target)</i></p>	<p>Increase the scientific basis for prioritizing Research and surveillance activities by increasing the number of risk assessments performed regarding antimicrobial products to two per year.</p>
14004	95%	<p>Assure that FDA inspections of domestic animal drug and feed manufacturing establishments, in conjunction with the timely corrections of serious deficiencies identified in these inspections, result in a high rate of conformance (at least 90 percent) with FDA requirements by the end of the fiscal year. 3</p>	<p>Assure that FDA inspections of domestic animal drug and feed manufacturing establishments and repackers, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high level of conformance (at least 90 percent) with FDA requirements. 3</p>
14005	<p>Calendar Year 1998: Salmonella Isolates: 1400 Human, 3500 Veterinary</p>	<p>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 National Antimicrobial Monitoring Program Database.</p> <p><i>Calendar Year 1999:</i></p>	<p>Maintain the bacterial isolate testing rate from human and animal origin in the National Antimicrobial Resistance Monitoring System (NARMS) database at 2,000 and 4,000 respectively</p>

		<i>Salmonella isolates: 2000 Human, 4000 Veterinary (target)</i>	
14006		Protect public health (human) and animal health by ensuring compliance with good manufacturing practices including the newly implemented BSE (Mad Cow Disease) regulation through education, regulatory inspections and industry/Federal/state partnerships.	
14007	75%	75 percent (target)	Maintain a 75 percent level for pre-submission conferences with industry sponsors.
14009	34%	Inspect 27 percent of registered animal drug and feed establishments. 1, 2	Meet the statutory biennial inspection requirement by inspecting 50 percent of registered animal drug and feed establishments.
14010	8000 ADE reports	<i>7,000 ADE reports (target)</i>	Maintain the number of Adverse Drug Event (ADE) reports reviewed at 7,000 through consumer participation in the pharmacovigilance program for veterinary drugs by publication and distribution of educational material.
14013	500 (target)	<i>600 (target)</i>	Properly target resources related to education and enforcement initiatives by maintaining the number of follow-up

			violative tissue residues investigations at 600 in targeted food producing animals.
14014		<i>Develop infrastructure</i>	Expand the geographical scope and capacity of the National Antimicrobial Resistance Monitoring System (NARMS) by the establishment of an international resistance database. 3
14015	Identified gaps in data	<i>Determine data base/systems to be integrated</i>	Improve our ability to monitor for Adverse Events by initiating the development of an integrated Agency-wide system. 3
14016	46	<i>50 (target)</i>	Increase bioresearch monitoring inspections completed and results received to 115.
14017	75%	<i>65% (target)</i>	Review and act on 65 percent of New Animal Drug Applications (NADAs)/Abbreviated New Animal Drug Applications (ANADAs) within 180 days of receipt.
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Medical Devices and Radiological Health	FY 1998 Actual: \$155,705.00	FY 1999 Current \$159,944.00	FY 2000 Request: \$186,051.00
15001	PMA's Only: 83% (estimate); PMA's & HDE's: 67% (estimate)	Maintain the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption (HDE) first	Increase the on-time percentage of Premarket Approval Application (PMA) first actions (within 180 days) and Humanitarian Device Exemption

		actions (within 75 days) completed at 65 percent. 1, 2	(HDE) first actions (within 75 days) completed from 67 percent in FY 1998 to 85 percent in FY 2000 and 95 percent by FY 2002.
15002	99.5%	Review and complete 90 percent of 510(k) (Pre-market Notification) first actions within 90 days. Expand third party 510(k) reviews and complete FDA action on 75% of them within 30 days. 1	Review and complete 95 percent of 510(k) (Pre-market Notification) first actions within 90 days.
15003	370 standards recognized.	Recognize over 415 standards for use in application review and update the list of recognized standards. 1	Update list of recognized standards.
15004	Apply to 16,000 to 20,000 reports (estimate)	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 1998 to over 25,000 in FY 1999. 1	Apply improved analytical methodology to approximately 30,000 manufacturer event reports, an increase of at least 20 percent over FY 1999.
15005.01	Class II and III domestic manufacturers only: 33% (estimate)	Inspect 26 percent of Class II and Class III domestic medical device manufacturers in FY 1999. 1, 2	Improve inspection coverage for Class II and Class III domestic medical device manufacturers from 26 percent in FY 1999 to 39 percent in FY 2000.
15005.012	Class II and III foreign manufacturers only: 14%	<i>Class II and III foreign manufacturers only: 12%</i>	Improve inspection coverage for Class II and Class III foreign medical device manufacturers from 12

			percent in FY 1999 to 19 percent in FY 2000.
15007	Less than 3% with Level 1 findings (estimate)	Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level I (serious) inspection problems.	Ensure that at least 97 percent of mammography facilities meet inspection standards, with less than 3 percent of facilities with Level 1 (serious) inspection problems.
15008	95% (estimate)	Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95 percent of identified high-risk, noncompliant or defective products within 30 days of discovery.	Maintain response to significant electronic product risk by initiating regulatory actions and recalls for 95 percent of identified high-risk, noncompliant or defective products within 30 days of discovery.
15009	86% (estimate)	70% (target)	Review and complete 85 percent of Premarket Approval Application (PMA) supplements for new indications within 180 days in FY 2000 and 95 percent by FY 2002.
15010	Identify priority materials for standards development.	<i>Initiate standards development</i>	Investigate correlation of device failures with aging biomaterials and provide quality assurance for device software. 3
15011	9,413	8900 (target)	Maintain annual inspection coverage for mammography facilities (8,900 inspections of a total of approximately 10,000 facilities) in FY 2000.
15012	Recruit 24 pilot facilities	<i>Evaluate pilot efforts</i>	Develop Sentinel Surveillance System for

			injury reporting based on approximately 75 to 90 representative user facilities.
15013		<i>Hold small group meeting to discuss problems.</i>	Develop baseline data to estimate problem and risk magnitude for marketed medical devices. 3
15014	72% (estimate)	65% (target)	Review and complete 85 percent of complex 510(k) (Pre-market Notification) final actions within 90 days in FY 2000 and 95 percent by FY 2002.
15015	65% (estimate)	65% (target)	Complete 95 percent of Investigational Device Exemption (IDE) "Agreement" meetings and Pre-market Approval Application (PMA) "Determination" meetings within 30 days.
15016	50% of inspection resources devoted to high-risk devices	Improve quality conformance of high-risk products like cardiovascular devices by committing over 75% of inspection resources to high risk devices.	Improve quality conformance of high-risk products like cardiovascular devices by committing over 90 percent of inspection resources to high risk devices.
15018	93%	Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of	Assure that FDA inspections of domestic medical device manufacturing establishments, in conjunction with the timely correction of serious deficiencies identified in these inspections, result in a high rate of

		conformance (at least 90 percent) with FDA requirements. 3	conformance (at least 95 percent) with FDA requirements. 3
15020	Signed the Mutual Recognition Agreement with the European Union.	<i>Chairing the Global Harmonization Task Force that seeks to harmonize regulatory requirements.</i>	Implement the Mutual Recognition Agreement (MRA) with the European Union (EU).
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
National Center for Toxicological Research	FY 1998 Actual: \$32,189.00	FY 1999 Current: \$31,579.00	FY 2000 Request: \$33,679.00
16001		Demonstrate a model toxicity knowledge base to support and expedite product review. 1	
16002	Utilized model animal and cell culture transgenic systems to evaluate risk to the human genome.	Develop better biological assays to measure genetic changes and predict human genetic damage. <i>Predict adverse human response to regulated products using model transgenic systems.</i>	Develop a new biological assay to measure genetic change and validate two existing models that predict human genetic damage.
16003	Conducted case-control molecular epidemiology studies to assess breast and prostate cancer in African-American women/men.	Complete biochemical and epidemiology studies to define the basis of susceptibility of humans to the toxicity of regulated products. <i>Identify subpopulations of humans at increased risk using molecular markers.</i>	Conduct molecular epidemiology studies to identify biomarkers of the most frequently occurring cancers in highly susceptible subpopulations.
16004	Computer-based predictive system was used to develop model for rodent and human hormone binding	Develop modeling tools to predict better risk for cancer, reproductive, developmental, neurological, genetic,	Validate a model computer-based predictive system to support and expedite product review of

	proteins.	and acute toxicological outcomes. 1 <i>Computer-based predictive systems being used to evaluate toxins.</i>	estrogenic or estrogen-like compounds.
16005	Report needed to regulate fumonisin B1 exposure in foods and long-term chloral hydrate usage completed. Began multi-generation studies of endocrine disrupters.	Support product review by developing faster, more accurate tests based on mechanisms of toxic actions. 1 <i>Continue two-year chronic bioassays on urethane in ethanol and malachite green. Begin studies to assess risk of alpha hydroxy acids and endocrine disrupters.</i>	Conduct studies that relate how a compound causes damage to the damage itself, in order to strengthen the scientific basis for regulation of compounds of FDA significance.
16006		Develop rapid and sensitive methods for identifying pathogens, foodborne bacteria, and microbial contaminants.	
16007	Presented, at a scientific forum, a unifying approach to safety assessments for both carcinogenic and non-carcinogenic effects. This addressed the uncertainty caused by extrapolating from high to low dose, from animals to humans, and from route and duration of exposure involved in estimating risk and setting acceptable exposure levels.	<i>Utilize risk assessments quantifying uncertainty in regulatory decisions.</i>	Develop partnerships with government, industry, and academic scientists to conduct studies that demonstrate cross-species comparability and eliminate assumptions necessary for extrapolating laboratory toxicity data to human disease.
16008	Screened animal products and environments for microorganisms	<i>Evaluate the mechanisms of competitive exclusions as a technique to</i>	Develop methods of predicting, more quickly and accurately, the risk associated with

	harboring antibiotic resistance.	<i>protect poultry products and explore dose-response models for assessing risk due to pathogenic exposure.</i>	foodborne pathogens.
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Tobacco	FY 1998 Actual: \$34,000.00	FY 1999 Current: \$34,000.00	FY 2000 Request: \$68,000.00
17001	FDA conducted approximately 39,439 compliance checks in FY 1998 and contracted to have approximately 189,000 compliance checks performed by September 1999 with FY 1998 funding.	Enter into contracts with all 50 states (or establish a federal investigatory force in those states which are unable or unwilling to contract with FDA), to conduct an average of 16,500 unannounced compliance checks each month of retail establishments that sell tobacco products.	Conduct 400,000 compliance checks and select certain sites to target for intensified enforcement efforts to determine the effectiveness of different levels of effort.
17002			Ensure the elimination of certain forms of advertising, especially outdoor advertising within 1000 feet of schools and playgrounds (including transit advertising) and specialty item distribution such as hats and tee shirts with tobacco logos.
17003	A survey was tested in two markets each in ten states in FY 1998. The results are analyzed and will be used to develop baseline data. Based on this limited survey of retailers: - 97% were aware of the FDA tobacco rule,	Conduct meetings and a multimedia campaign, including point-of-purchase, radio, outdoor advertising, and newspapers, to educate retailers and other stakeholders about their obligations under the FDA tobacco rules and	Maintain the percentage of known retailers of cigarettes and smokeless tobacco products who are aware of the FDA tobacco rule at no less than 90 percent and increase the percentage of retailers who understand the age

	<p>- 84% were aware that the legal age for purchase is age 18,</p> <p>- 31-34% were aware that they had to check the ID of every customer under the age of 27.</p>	the impact of the rules.	and ID provisions of the rule to 50 percent.
17004	In FY 1998, approximately 400,000 retailer kits had been mailed.		Promote availability of free FDA retailer information kits, used to remind customers and young people about the requirements of the FDA tobacco rule, to at least 400,000 retailers of cigarettes and smokeless tobacco products and provide kits to those who request them.
17005		Design and, to the fullest extent permitted under any court orders addressing such activities, begin to implement a regulatory program for cigarettes and smokeless tobacco products, including: Begin to examine the appropriate scientific and regulatory framework to evaluate products that state or imply that they are less hazardous; Assist other agencies within the Department of Health and Human Services in providing the Federal Trade Commission with an analysis of the public health issues associated with the testing and	To the fullest extent permitted under any court order, establish the scientific and regulatory framework to address the challenges posed by new and novel nicotine-containing tobacco products as well as issues raised by current products and replacement therapies.

		reporting of the tar and nicotine content of the smoke of cigarettes; and Establish an evaluation and review procedure for new products.	
17006		<i>Baseline data is being developed as the compliance check program is being implemented.</i>	Conduct follow-up compliance checks of 100 percent of retailers found to be in violation of the rule.
	<u>1998 Actual Performance</u>	<u>FY 1999 Performance Goal</u>	<u>FY 2000 Performance Goal</u>
Imports	Resources associated with import regulation are included in Program sections.		
18002		<i>Complete design specifications for an analysis that is intended to profile variations in criteria used by different FDA programs in screening import entries.</i>	Complete analysis of variations in criteria used by FDA programs to screen import entries. Establish Agency screening guidelines that emphasize risk-based decisions through program information. 3
18005	Preliminary checks done on filers to determine need for more complete filer evaluation.	<i>Complete survey design intended to determine the accuracy rate of import entry data submitted to FDA.</i>	Complete survey of filers that submit import entry data electronically to FDA, and determine the error rates and error types that are representative of the population of filers. 3

Notes:

1. Goal was included in the Food and Drug Administration Modernization Act of 1997 (FDAMA): FDA Plan for Statutory Compliance (Issued: November 1998). Plan can be found at www.fda.gov/oc/fdama/fdamapln/ or www.fda.gov/oc/fdama/fdamapln/fdamapln.pdf

2. The target for this goal has been modified since the Food and Drug Administration Modernization Act of 1997 (FDAMA): FDA Plan for Statutory Compliance was issued.

3. Developmental Goal (performance goal has been identified, but the measure, data sources or data systems needed to define baselines and set performance targets are being developed).

APPENDIX 3: FDA'S IMPORT STRATEGY

The goal of FDA's import program is to assure that all FDA-regulated imports available to U.S. consumers are safe. The scope of the program is broad, covering all FDA-regulated products, which represent 30 percent of all imports into the U.S. The number of FDA-related import shipments reached nearly 4 million in 1997, continuing a 4 percent annual growth rate in the last decade. And the complexity is increasing--the reality of a truly global economy is adding significant regulatory challenges for FDA.

FDA's challenges include assuring safety of products from increasingly diverse countries of origin, with wide variation in technological capability of production sources; dealing with a higher percentage of semi-finished or finished goods; detecting known and emerging pathogens; and working in an evolving system of international trade and regulatory agreements. FDA's imports activities are focused on the establishment of a safety net that extends from the point of production in source countries through their entry into the U.S. To ensure that its safety net works, the Agency employs three strategies:

- **Reduce the probability that violative products will be exported to the U.S.** This is accomplished through multiple strategies, including educational and technical assistance targeted to foreign producers and governments, foreign inspections, development of mutual recognition agreements (MRAs), participation in international standard-setting forums, and establishment of international data bases that adopt a global focus on health risks. In public meetings conducted during the summer of 1998 as part of the FDA Modernization Act planning process, FDA's stakeholders expressed strong support for FDA's international activities. They were particularly vocal in advocating FDA's presence at the prevention end of the import chain. For example, stakeholders felt that FDA should have a prominent "seat at the table" in standard-setting bodies such as *Codex Alimentarius* (for foods), and should negotiate MRAs that promulgate high safety and quality standards while promoting trade. Proactive stances taken by FDA in these settings will raise the probability that imports reaching the U.S. are safe. Stakeholders encouraged FDA to staunchly defend the U.S. standard of health and safety both in determining standards equivalency and in assuring that foreign nations have the regulatory systems in place to meet those standards. FDA will view high public health standards as its highest priority as it participates in the ongoing development of international agreements and multi-national standard setting.

- **At the border, make rapid and reliable decisions on product entry.** In order to operate at high confidence levels, FDA has established a system that prioritizes entries based on degree of presumed risk. More than half of all entries are now allowed to proceed into the U.S. within minutes of their arrival without direct examination of the product. This is possible because information on the history of the product, importer and source country is collected and used to screen for potential risk. These rapid entry decisions are called "immediate may proceed" decisions and are based on screening criteria developed by FDA. The remainder of entries are reviewed by Agency staff, using more sophisticated screening criteria and more detailed product information. Most of these are allowed entry within hours. Thus, a majority of all import entries are allowed entry without visual or physical examination, and with high levels of confidence of their safety.
- **Target violative products at the border and prevent their entry.** A small percent of import entries (approximately 2 percent) are directly assessed, through field examinations, and, in less than 1 percent of the cases, through laboratory analysis. The need to directly examine this small portion of imports is based on empirical evidence that selected product categories from certain source countries or shippers have shown significant violation rates. In addition, surveillance examination of imported products is necessary to identify new problem firms or emerging health concerns. Certain violative firms and products with poor histories of compliance are subject to detention without physical examination at the border until the importer can prove the product complies with FDA standards. FDA will continue to refine and standardize its risk-based criteria for screening imports as more comprehensive information concerning the product and country of origin are entered into the automated review system.

Performance goals for FY 2000 support the continued implementation of the above three strategies. 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. A specific target for the medical device program in FY 2000 is to implement a Mutual Recognition Agreement with the European Union. These activities will assure that products from those nations are meeting FDA standards. The Agency has also planned for an increasing number of foreign inspections, particularly for food and medical device establishments. These inspections will be focused on those establishments that represent major sources of imports to the U.S. and/or that produce higher-risk products.

To maintain high assurance that the vast majority of imports are safe upon entry, FDA will continue to strengthen the automated import information system so that more robust information can be brought to bear on the decision to allow imports to proceed. FDA will also focus on the accuracy of the information used in the system. In order to assure that import entry information is being accurately recorded the agency will evaluate filers of electronic import data to determine error rates. Once baseline data are established, FDA will establish an error reduction goal and embark on intervention strategies to reduce the error rate.

To support the targeting of suspect products, FDA will continue to conduct laboratory analysis on a small percentage of products with potential problems (less than 1 percent of entries). It will, however, be extremely difficult to maintain even that percentage, given no increase in import resources coupled with continued rapid growth in the volume of import entries. The Agency has established an FY 2000 performance goal to evaluate the variation in criteria used to screen import entries in different product areas, and to aim for an efficient system that applies consistent, risk-based decision rules across import categories. This will provide the potential for greater convergence in determining what represents high risk to the U.S. consumer.

Performance Goals, Data Sources, and Baselines:

Goal Statement: Implement the Mutual Recognition Agreement (MRA) with the European Union (EU). (See [Devices](#) program section in Plan.)

Goal Statement: Expand the geographical scope and capacity of NARMS by the establishment of an international resistance database. (See [Veterinary Medicine](#) program section in Plan.)

Goal Statement: Improve inspection coverage for Class II and Class III foreign medical device manufacturers from 12 percent in FY 1999 to 19 percent in FY 2000, and increase the number of inspections/evaluations of foreign food establishments from 100 to 250. (See [Devices](#) and [Foods](#) program sections in Plan.)

Goal Statement: Complete survey of filers that submit import entry data electronically to FDA, and determine the error rates and error types that are representative of the population of filers.

Data Source: ORA, Division of Import Operations and Policy

Baseline Data:

FY 1998:

Preliminary checks done on number of filers to determine need for more complete filer evaluation.

FY 1999:

Complete survey design intended to determine the accuracy rate of import entry data submitted to FDA.

Goal Statement: Complete analysis of variations in criteria used by FDA programs to screen import entries. Establish Agency screening guidelines that emphasize risk-based decisions through program information.

Data Sources: ORA, Operational and Administrative System for Import Support (OASIS) records

Baseline Data:

FY 1999:

Complete design specifications for an analysis that is intended to profile variations in criteria used by different FDA programs in screening import entries.

APPENDIX 4: GLOSSARY OF ACRONYMS

510(k): Premarket notification for medical devices substantially equivalent to products already on the market

AADA: Abbreviated Antibiotic Drug Application

ADE: Adverse Drug Event

ADAA: Animal Drug Availability Act of 1996

ADR: Adverse Drug Report

AERS: Adverse Events Reporting System

AHI: Animal Health Institute

AIDS: Acquired Immune Deficiency Syndrome

ANDA: Abbreviated New Drug Application

ANSI: American National Standards Institute

BLA: Biologic License Application

BLT: Blood Logging and Tracking System

BRFS: Behavioral Risk Factors Survey

BRMS: Biologics Regulatory Management System

BSE: Bovine Spongiform Encephalopathy (Mad Cow Disease)

CARS: Compliance Achievement Reporting System

CBER: FDA Center for Biologics Evaluation and Research

CDC: Centers for Disease Control and Prevention

CDER: FDA Center for Drug Evaluation and Research

CDRH: FDA Center for Devices and Radiological Health

CFSAN: FDA Center for Food Safety and Applied Nutrition

CGMPs: Current Good Manufacturing Practices

CJD: Creutzfeldt-Jakob disease

COMIS: Center-wide Oracle Management Information System

COMSTAT: Compliance Status Information System

CRADA: Cooperative Research and Development Agreement

CRS: Contamination Response System

CSTE: Council of State and Territorial Epidemiologists

CMC: Chemistry, Manufacturing, and Controls

CVM: FDA Center for Veterinary Medicine

DHHS: Department of Health and Human Services

DNA: Deoxyribonucleic acid

DOD: Department of Defense

DoL: Department of Labor

DRLS: Drug Registration and Listing System

DSHEA: Dietary Supplement Health and Education Act

EDR: Electronic Document Room

EDMS: Electronic Data Management System

EIR: Establishment Inspection Report

ELA: Establishment License Application

EPA: Environmental Protection Agency

ERS: Economic Research Service

ETS: Environmental Tobacco Smoke

EU: European Union

FACTS: Field Accomplishment and Compliance Tracking System

FAO: United Nations Food and Agricultural Organization

FAS: USDA Foreign Agriculture Service

FDAMA: Food and Drug Administration Modernization Act of 1997

FD&C Act: Federal Food, Drug and Cosmetic Act

FORCG: Food Outbreak Coordination Response Group

FPLA: Fair Packaging and Labeling Act

FSI: National Food Safety Initiative

FSIS: Food Safety Inspection Service (USDA)

FTC: Federal Trade Commission

FTE: Full-time equivalents

FY 1999: Fiscal Year 1999 (October 1998 - September 1999)

GAO: Government Accounting Office

GAPs: Good Agricultural Practices

GATT: General Agreement on Tariffs and Trade

GPRA: Government Performance and Results Act of 1993

GMPs: Good Manufacturing Practices

GRAS: Generally Recognized as Safe food ingredients

GSFA: General Standards for Food Additives

HACCP: Hazard Analysis Critical Control Points (a quality assurance and inspection technique)

HDE: Humanitarian Device Exemption

HUD: Humanitarian Use Device

ICH: International Conference on Harmonization

IDE: Investigational Device Exemption

INAD: Investigational New Animal Drug

INADA: Investigational New Animal Drug Application

IND: Investigational New Drug

ISO: International Standards Organization

IT: Information technology

JIFSAN: Joint Institute for Food Safety and Applied Nutrition

LACF: Low Acid Canned Foods

LAN: Local Area Network

MDR: Medical Device Reporting system

MOU: Memorandum of Understanding

MPRIS: Mammography Program Reporting and Information Systems

MQSA: Mammography Quality Standards Act

MRA: Mutual Recognition Agreement

NADA: New Animal Drug Application

NAFTA: North Atlantic Free Trade Agreement

NAFTA TWG: North American Free Trade Agreement Technical Working Group

NARMS: National Antimicrobial Resistance Monitoring System

NASS: National Agricultural Statistics Survey

NCI: National Cancer Institute

NCTR: FDA National Center for Toxicological Research

NDA: New Drug Application

NDE/MIS: New Drug Evaluation Management Information System

NIDA: National Institute on Drug Abuse

NIEHS: National Institute for Environmental Health Sciences

NLEA: Nutrition Labeling and Education Act

NME: New Molecular Entity

NPR: National Partnership for Reinventing Government

NSE: Not substantially equivalent determination

NTP: National Toxicology Program

OASIS: Operational and Administrative System for Import Support

ORA: FDA Office of Regulatory Affairs

OSHA: Occupational Safety and Health Administration

OTC: Over-the-counter

OTR: Office of Testing and Research (CDER)

PAS: FDA Public Affairs Specialist

PDUFA: Prescription Drug User Fee Act of 1992

PIFSI: Produce and Food Safety Initiative

PLA: Product License Application

PMA: Premarket Approval (Application to market medical device that requires premarket approval)

PODS: Project-Oriented Data System

PQRI: Product Quality Research Initiative

RGHSA: Radiation Control for Health and Safety Act

REGO: Reinventing government initiative

RIMS: Regulatory Information Management Staff

RVIS: Residue Violation Information System

SAMHSA: Substance Abuse and Mental Health Services Administration

SN/AEMS: Special Nutritionals Adverse Events Monitoring System

STARS: Submission Tracking and Review System

StmDT104: Salmonella typhimurium DT 104

TRIMS: Tissue Residue Information System

UMCP: University of Maryland-College Park

USDA: United States Department of Agriculture

VFD: Veterinary Feed Directive

WHO: United Nations World Health Organization

WTO: World Trade Organization
