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**BEFORE THE SUBCOMMITTEE ON AGRICULTURE,
RURAL DEVELOPMENT,
FOOD AND DRUG ADMINISTRATION,
AND RELATED AGENCIES
U.S. HOUSE OF REPRESENTATIVES**

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INTRODUCTION

Chairman Kingston, Ranking Member Farr and members of the Subcommittee, I am Dr. Margaret Hamburg, Commissioner of the U.S. Food and Drug Administration. I am pleased to present the President's fiscal year 2013 budget request for the Food and Drug Administration (FDA).

I want to begin by thanking you for your efforts over the past few years to shrink the gap between the agency's budget and its vast and evolving responsibilities. As a science-based regulatory agency of global scope, FDA's mission is both exciting and daunting. Our core responsibilities are evolving and expanding to include additional product areas such as tobacco, to accommodate scientific and technological advances, and to step up to the global leadership role that FDA must play if we are to promote innovation and protect the American consumer.

Our recent spending and new budget requests reflect this evolution. As you will see, we are embracing these changes in several important ways -- by deploying smarter and more flexible regulatory approaches, by identifying efficiencies and innovative approaches to our core mission activities that improve outcomes and better target our resources, and by using collaborations to leverage expertise, data, and experience. Through these new approaches, we are already improving efficiency and achieving concrete results. While the challenges loom large, we are confident that we have identified investments and approaches that will allow us to continue this evolution and to fully protect and promote the public health.

1. Concrete Investments = Concrete Results

With the funding you have provided, we have delivered significant and quantifiable benefits to the American people, and we are very proud of these achievements.

FDA now has the highest first action approval rate for new drugs we have ever had, and we continue to look for ways to improve the predictability, consistency and transparency of our drug review process. In FY 2011, we approved 35 innovative drugs, many of them ground breaking. This performance was among the highest number of approvals in the past decade, surpassed only by 2009. We lead the world in the number and speed of drug approvals: of the 57 novel drugs approved by both FDA and the EU between 2006 and 2010, 75% were approved first in the United States. All 23 cancer drugs approved by FDA and the EU were approved first in the United States. Last year also saw breakthroughs in personalized medicine, including two novel drugs that were developed and approved with diagnostic devices that will allow doctors to target the drug to those patients most likely to respond.

To achieve these results, and speed access for the American people, we made use of accelerated approvals and flexible clinical trial requirements and made sure manufacturers know that marketing applications can be based solely on foreign clinical data that meets certain clear and specific standards.

On the device side, in 2011, FDA released the [Plan of Action for Implementation of 510\(k\) and Science Recommendations](#), 25 specific actions that we would take in 2011 to improve the predictability, consistency, and transparency of our premarket programs. 75% of those actions, plus eight additional actions, are already completed or well underway. We issued guidance on the Agency's regulatory expectations for personalized medicine diagnostic devices that are developed along with a therapeutic product, to target that therapeutic product to the appropriate population. We launched the [Innovation Initiative](#), which proposed actions that the Agency could take to help accelerate and reduce the cost of development and regulatory evaluation of innovative medical devices in a way that maintains or improves patient safety and is based on sound science.

We also have successfully prevented at least 114 drug shortages. FDA has sent letters to pharmaceutical manufacturers, reminding them of their legal obligations to report certain discontinuances to the Agency, and urging them to voluntarily notify FDA of all potential disruptions of the prescription drug supply, even when not required by law. This has resulted in a significant increase in the number of potential shortages reported to FDA, and thus enhanced our ability to take action. Just last week, we announced a series of steps to increase the supply of critically needed cancer drugs that were in short supply, including exercising enforcement discretion to allow temporary importation of a replacement drug and approving a new manufacturer on an expedited basis.

We are also playing our part to address the rising costs of health care, by implementing a new approval pathway for biosimilar biological products and a user fee program to support review and evaluation of biosimilar products. We are also proposing a new generic drug user fee program that will support faster, more predictable reviews for generic drugs, that will effectively eliminate the current generic application backlog, and that will help assure quality by providing resources for regular surveillance inspections of manufacturers of generic drugs.

The FDA Food Safety Modernization Act (FSMA), the most sweeping reform of our food safety laws in more than 70 years, was signed into law by President Obama on January 4, 2011. We have already issued interim final rules describing criteria for administrative detention of adulterated products and have used this authority several times. We met the FSMA mandate for foreign food safety inspections, and are well on the way to meeting the 5-year inspection frequency mandate for high-risk domestic food facilities. We also have issued a new guidance to the seafood industry on food safety hazards. We anticipate issuing several proposed rules called for in FSMA shortly. We post regular progress reports on implementation milestones on our web site.

Since enactment of the Tobacco Control Act of 2009, we have been working to achieve four goals: to prevent youth from using tobacco; to help adults who use tobacco to quit; to provide accurate information on the contents of tobacco and consequences of tobacco use to the public; and to use regulatory tools, including tobacco product standards, to reduce the public health burden of tobacco in the United States. To that end, we have created the new Center for Tobacco Products, which is already enforcing a ban on cigarettes with characterizing flavors (other than menthol), enforcing requirements for new warnings on smokeless tobacco products, and restricting youth access to cigarettes.

We have established a world-class testing laboratory with expertise and capacity to increase our understanding of the health risks of these products, and have supported innovative research on the impact of altering nicotine levels in tobacco products.

In June, FDA issued our “Pathway to Global Product Safety and Quality” report, describing the challenges of regulating in the globalized world in which FDA now operates, calling for a paradigm shift in how we approach our duties in light of such challenges, and describing the concrete actions we will take in four areas: 1) assembling global coalitions of regulators dedicated to building and strengthening the product safety net around the world; 2) developing a global data information system and network in which regulators worldwide can regularly and proactively share real-time information and resources across markets; 3) expanding FDA’s capabilities in intelligence gathering and use, with an increased focus on risk analytics and thoroughly modernized IT capabilities; and 4) effectively allocating agency resources based on risk, leveraging the combined efforts of government and industry. The essence of this strategy marries creative international coalitions with cutting-edge investigative tools to continue to provide the consistently high level of safety and quality assurance the public expects—and deserves.

In all that we do, we are guided by science, by our obligation to the American people to be innovative and efficient and, most important, by our mission to protect and promote the public health.

2. Maximizing the Impact of Agency Funds

At this time of fiscal restraint, it is more important than ever to focus on our core functions and to actively look for opportunities to streamline activities and leverage human and financial resources.

Focusing on our core functions means recognizing how those functions are evolving, and substantially changing the agency’s operating model to address the scientific, technologic, and globalization challenges of the 21st century. To this end, I have instituted a series of reorganizations designed to ensure that the agency better reflects its evolving responsibilities, but that also recognizes our responsibility to make the most efficient use of our limited resources. Early in my tenure, I appointed a new Deputy Commissioner for Foods, to ensure coordination of our growing and rapidly evolving responsibilities for oversight of the domestic and global food supply chain. Building on that success, last year I created the new position of Deputy Commissioner for Global Regulatory Operations and Policy, to fully recognize the need to integrate domestic and foreign inspections, streamline procedures, and seek greater harmonization and opportunities for collaboration with our counterparts in other countries. I also appointed a new Deputy Commissioner for Medical Products and Tobacco, reflecting our recognition that the review of medical products increasingly cuts across Center boundaries and that a new framework was necessary to address challenges like personalized medicine and combination products. Together, these changes build efficiencies into our organizational structure from the ground up and will make it easier to identify new opportunities for streamlining in the years to come.

We have made significant progress in consolidating our IT infrastructure into modern data centers. Simultaneously, we have modernized and standardized our hardware and software infrastructure, resulting in savings in power consumption and the ability to use FDA equipment and IT support resources more efficiently. You will see savings from this consolidation reflected in our proposed budget for FY 2013, as well as additional proposed savings.

We have expanded our efforts to leverage both financial and human capital through collaborations with public and private partners. For example, we recently entered a new collaboration with the European Medicines Agency (EMA) for shared efficiencies in our inspection programs for human and veterinary pharmaceutical products. Our Center for Drug Evaluation and Research is working in partnership with the Critical Path Institute, an independent, publicly funded institute, to establish public-private consortia to address key questions in regulatory science. And FDA's Center for Tobacco Products is partnering with the Environmental Protection Agency's eRulemaking program to develop a web-based tool to improve access to and participation in the federal regulatory process.

Another key area for improved efficiencies is improved targeting of inspection resources. We have been working hard to ensuring that our import inspection programs are risk-based, for the most efficient targeting at port-of-entry. We are redeploying current food inspection resources and pursuing efficiencies to support initial implementation of FSMA.

3. Preparing FDA for the Challenges Ahead

FDA's mission is challenging, even in the best of times, with scientific advances occurring at breakneck speed, and the pace of globalization accelerating. Our responsibilities are vast and growing, a trend that will only continue. We receive thousands of medical product submissions each year, and serve as the watchdog for the tens of thousands of products on the market to be sure they continue to meet the highest standards.

We have evolved from a country that once consumed simple, primarily domestically-produced goods to one that consumes complex products manufactured in every corner of the globe. We enjoy a greater variety of products from a greater range of places than ever before. The complexity of the products we regulate and the complexity of the supply chains by which they reach the eventual consumer has only increased. All of this means that FDA's job has gotten more complex and the stakes have continued to increase.

As our FY 2013 budget points out, imports of FDA-regulated food products come from more than 300,000 foreign facilities in 200 countries. Nearly 40% of the drugs Americans take are made overseas, and about 80% of active pharmaceutical ingredients are imported. Approximately half of medical devices used in the United States come from abroad. Food imports have increased nine-fold since 1993. About seventy percent of seafood and about 35 percent of fresh produce consumed in the United States comes

from foreign countries. At the Port of Savannah alone, the entering lines of FDA regulated product jumped from 20,000 in 2002 to 158,000 last year.

FDA oversees the safety of four-fifths of the nation's food supply. The public needs to know that industry and the government are using the best modern tools to prevent problems. According to the CDC, this country sees 48 million foodborne illnesses occur every year resulting in 128,000 hospitalizations and 3,000 deaths, with an aggregated annual cost of illness of \$77.7 billion

We are grateful that Congress has begun to help give FDA the tools needed to effectively regulate in a modern, complex, globalized environment. We are on the right path, but the road is long and challenging. The proposed FY 2013 budget, described in more detail below, will continue the forward motion that you have supported.

4. Next Steps: Investing in FY 2013

At the end of this Fiscal Year, FDA's drug and device user fee programs will expire. These programs make it possible for FDA to ensure the safety, effectiveness and quality of the nation's medical products. But they do far more. The user fee proposals you see in our FY 2013 budget, both those reauthorizing existing programs and those authorizing new programs, reflect time spent this past year listening to all our stakeholders and coming to agreement with them, not only on the scope but also on the direction these programs should take to best promote and protect the public health.

In this budget, you will see our commitment to smart regulation and efficacy in medical product review. We propose investment in improved standardization of electronic submissions for drugs, and modernization of FDA's food-related data bases and data sharing systems. Proposals for smarter engagement with Chinese regulators will allow FDA to make better evidence-based decisions and allocate FDA resources based on risk. We propose a new focus on potential uses of meta-analysis for drugs, and streamlined review goals for medical devices.

Enhanced communication and additional guidance development across all our user fee programs will further enhance both efficiency and transparency. Public workshops to discuss frameworks for evaluating benefits and risks will provide further transparency, as well as smarter regulatory action. For the proposed new user fee program for generic drugs, transparency means requiring the identification of facilities involved in the manufacture of generic drugs and associated active pharmaceutical ingredients, and improving FDA's communications and feedback with industry.

Our commitment to fostering innovation is woven into the fabric of this budget. For example, we propose to augment our clinical pharmacology and statistical capacity to address drug applications that rely on biomarkers. We propose deployment of hand-held mobile devices for food inspections, and a new laboratory facility that will support cutting-edge regulatory science.

FDA is often the last line of defense between the consumer and unsafe medical and food products. That is why, in this budget, you will see our commitment to significant safety initiatives. These include the first cosmetic user fee program to strengthen FDA's efforts to ensure the safety of cosmetics and remove unsafe cosmetics from the market. Our PDUFA V proposal includes the Sentinel Initiative, FDA's effort to develop an active post-market drug safety surveillance capacity through evaluation of post-market safety signals in population-based databases. Enhanced engagement with our regulatory counterparts in China will broaden the range of our inspections, allow follow up inspections, and foster improved interactions intended to improve the safety and quality of food and medical products.

Just as the food supply of 2002 is not the food supply of today, so too the FDA of 2002 must not be the FDA of today. That is why, in this budget, you will see our commitment to building a strong and reliable food safety system, focused on prevention and leveraging the valuable work of our partners in state and local governments. FSMA requirements represent rare consumer-industry consensus on food safety goals and the means of achieving them – in this budget we must commit to a new user fee program that can make these shared goals a reality. Food safety gives peace of mind to every family.

These are just a few examples of the many ways that our proposed FY 2013 budget reflects our commitment to innovative, efficient, and transparent approaches to our public health mission. Our full Fiscal Year 2013 Budget Request follows.

FOOD AND DRUG ADMINISTRATION FISCAL YEAR 2013 BUDGET REQUEST

I. FY 2013 Budget Summary

The FY 2013 budget recommends \$4.5 billion for FDA, a 17 percent increase from FY 2012. The FY 2013 increase for user fees, including increases for current law user fees and amounts for seven new user fee programs, accounts for 98 percent of the FDA budget increase.

FDA user fee programs support safety and effectiveness reviews of human and animal drugs, biological products, medical devices, and other FDA-regulated products. Fees also allow FDA programs to achieve timely and enhanced premarket review performance. Finally, fees support the programs and operations of the FDA Center for Tobacco Products

For FY 2013, FDA is proposing cuts in two areas – information technology (IT) and the FDA Buildings and Facilities (B&F) account. In addition to these budget authority reductions, FDA is also absorbing more than 80 percent of the inflationary cost of rent activities.

After accounting for these savings, the net increase in budget authority is \$11.5 million for FY 2013. Our increases support import safety, medical countermeasures, White Oak laboratory facilities, a portion of the increased cost of our rent activities, and the military pay raise that FDA Commissioned Corps officers will receive.

The federal investment in FDA is small compared to the breadth of our mission and the \$2 trillion in products that we regulate. The investment in FDA is also an investment in the economic health of two of the largest sectors of America's economy: the U.S. food industry and the medical products industry.

II. FDA Budget Authority

A. FY 2013 Reductions

FDA made significant progress in recent years to consolidate our IT infrastructure into modern data center facilities. During the consolidation, FDA modernized and standardized its hardware and software infrastructure. This effort provides an FDA computing environment that reduces our costs and provides agility not previously possible. The result is savings in power consumption and more efficient use of FDA equipment and resources for IT support.

Under this FY 2013 initiative, FDA will realize savings that flow from the consolidation effort. FDA will generate additional IT savings by streamlining other data management activities, reducing redundant IT devices, and reducing other IT costs, for a total savings of \$19.7 million. Finally, FDA will also save \$3.5 million by deferring repair and maintenance projects supported by our Building and Facilities account.

B. Food and Drug Imports from China

FDA is requesting a budget authority increase of \$10 million to strengthen the safety of foods, drug products and ingredients exported from China to the United States. During the past decade, the global economy has been shaped by a number of powerful forces, including a rapidly increasing flow of goods into the United States. These foreign goods often follow complex paths through multi-step supply chains to reach the United States.

This dynamic is very evident in our trade with China. From FY 2007 to 2011, the number of shipments of FDA-regulated products from China increased by 62 percent. This represents a fundamental change in our economic and security landscape, a change that requires FDA to alter its approach to protecting the health of the American public. To address this change, FDA must strengthen its capacity to inspect Chinese facilities that ship products to the United States and strengthen its ability to perform risk analysis on FDA-regulated products from China.

The addition of \$10 million will strengthen FDA's ability to protect American consumers and patients in important and fundamental ways.

- FDA will improve its food and drug inspection and analytical capabilities by increasing its presence in China with 16 inspectors, and by adding three U.S.-based analysts.
- FDA will broaden the range of its inspections. In addition to inspecting Chinese facilities that manufacture food and medical products for export to the United States, FDA will inspect sites of clinical trials. FDA will also conduct follow-up inspections to ensure that firms continue to manufacture food and medical products under safe conditions.
- FDA will strengthen the understanding of Chinese regulators and the exporting industry about U.S. safety standards through targeted workshops and seminars. This process will foster a constructive dialogue on the critical role of inspections and other approaches for improving the safety and quality of food and medical products.

FDA views this initiative as a unique opportunity to engage the Chinese industry and our regulatory counterparts in China. Through this initiative, Chinese regulators will enhance their understanding of FDA requirements and strengthen their regulatory capacity to assure the safety of the food and drugs that their industries export to the United States. With these resources, FDA will develop more robust knowledge about the complexities of regulatory pathways and supply chains within an increasingly globalized environment. This understanding will allow FDA to make better evidence-based decisions and allocate FDA resources based upon risk.

C. FDA Medical Countermeasures Initiative

The FDA Medical Countermeasures Initiative (MCMi) is designed to help meet America's national security and public health requirements for medical countermeasure (MCM) readiness. MCMs include drugs, vaccines, diagnostics, and other medical products needed to respond to chemical, biological, radiological, nuclear (CBRN) threats and emerging infectious diseases.

Thanks to the efforts of this subcommittee, FDA received an appropriation of \$20 million in FY 2012 to provide a base of funding for FDA's MCMi. For FY 2013, the FDA budget includes an additional \$3.5 million for FDA medical countermeasures activities.

With the FY 2012 base funding and the additional FY 2013 resources, FDA will support partnerships with industry, academia, and government partners to improve the development timelines and success rates for MCMs. FDA will also expand technical assistance to developers of the highest priority MCMs.

The top priorities for these MCM funds include FDA action teams to support the development of MCMs to address the following priorities:

- warfighter care for American soldiers exposed to trauma or CBRN threats
- diagnosing and treating the multiple manifestations of acute radiation syndrome

- meeting the special needs of pediatric patients and pregnant women
- developing next generation in vitro diagnostic tests for CBRN threats
- working closely with HHS to establish flexible manufacturing capacity in the U.S.

Since the announcement of the FDA MCMi in August 2010, FDA and its drug, device and biologics programs have worked aggressively to ensure that the United States has access to high-priority MCMs during a public health emergency. Our accomplishments to date include:

- issuing a five-year strategic plan for the MCMi
- launching a rigorous MCM regulatory science program
- sponsoring an Institute of Medicine workshop on the challenging scientific issues related to MCM development
- establishing a partnership with the Defense Advanced Research Projects Agency (DARPA) to collaborate on regulatory science research
- hosting a meeting of state and local public health leaders to address emergency preparedness and response
- conducting public workshops and advisory committee meetings to advance development of high priority MCMs
- initiating threat briefings to ensure that FDA reviewers are fully aware of the threats – and therefore the risks – as they conduct benefit- risk analyses on MCM products.

D. FDA Regulatory Science Facilities

On August 18, 2010, the General Services Administration (GSA) awarded the construction contract for the new laboratory complex at White Oak, and construction is well underway.

An FY 2013 increase of \$17.7 million will allow FDA to outfit the new CBER-CDER Life Sciences-Biodefense Laboratory complex that will support FDA's core regulatory science needs. FDA must make this investment now to ensure that all laboratory biosafety hazard systems are operational and the laboratory is ready for occupancy during FY 2014.

As GSA completes construction of the Life Sciences-Biodefense Laboratory complex, FDA's FY 2013 budget request contains resources to make the facilities operational and to fully certify the new laboratory. The new laboratory is essential to support more efficient development of new and innovative medical products and to better assess product safety and effectiveness. With these resources, FDA will operate in modern laboratory facilities that allow FDA to fulfill FDA's public health responsibilities.

E. Pay and Rent

The FY 2013 budget also contains \$1.5 million to support the military pay increase for Commissioned Corps personnel that serve at FDA and \$2.0 million to pay a portion of

the inflationary rent costs for FDA food safety and nutrition programs. Funding these elements of the FY 2013 budget will help ensure that FDA can retain the professional staff to perform our mission of protecting patients and consumers and improving public health.

III. FDA User Fees

A. Prescription Drug User Fees

PDUFA History and Background: The timely review of the safety and effectiveness of New Drug Applications and Biologics License Applications is central to the FDA mission to protect and promote the public health. Before PDUFA was enacted by Congress in 1992, FDA's review process was understaffed, unpredictable, and slow. FDA lacked sufficient staff to perform timely reviews or develop procedures and standards to make the process more rigorous, consistent, and predictable. Access to new medicines for U.S. patients lagged behind other countries.

In response to concerns expressed by industry and patients, Congress enacted PDUFA, which provided additional funds through user fees to allow FDA to hire reviewers and support staff and to upgrade FDA information technology systems. At the same time, FDA committed to complete application reviews in a predictable time frame. These changes revolutionized the drug approval process in the United States and allowed FDA to speed the application review process for new drugs, without compromising the FDA's high standards for demonstrating safety, efficacy, and quality of new drugs prior to approval.

PDUFA Achievements: Through PDUFA, FDA has received a stable, consistent source of funding that allows FDA to focus on promoting innovative therapies and on bringing critical products to market. Since Congress enacted PDUFA in 1992, this user fee program has provided patients with faster access to more than 1,500 new drugs and biologics. These new drugs and biologics include treatments for cancer, infectious diseases, neurological and psychiatric disorders, and cardiovascular diseases.

FY 2011 PDUFA Performance: During FY 2011, FDA approved 35 new, groundbreaking medicines, including two treatments for hepatitis C, a drug for late-stage prostate cancer, the first drug for Hodgkin's lymphoma in 30 years, and the first drug for lupus in 50 years. Of the 35 innovative drugs approved in FY 2011, 34 met their PDUFA target dates for review.

Reversal of the Drug Lag: As these statistics demonstrate, PDUFA has led to the reversal of the drug lag that prompted Congress to adopt this law. Since the enactment of PDUFA, FDA has steadily increased the speed of Americans' access to important new drugs compared to the European Union (EU) and the world as a whole. Of the 35 innovative drugs approved in FY 2011, 24 (nearly 70 percent) were approved by FDA before any other regulatory agency in the world, including the European Medicines Agency. Of 57 novel drugs approved by both FDA and the EU between 2006 and 2010, 43 (75 percent) were approved first in the United States.

Prompt Approval and Launch of New Drugs: In recent years, the average FDA drug review time also has been significantly faster than those in the EU. For priority drugs approved between 2006 and 2010, FDA's median time to approval was six months (183 days). This is more than twice as fast as the EU time to approval for those drugs, which took a median time of 13.2 months (403 days). For standard drug reviews, FDA's median time to approval was 13 months (396 days), which is 53 days faster than the EU time to approval of 14.7 months (449 days) for those drugs.

Providing Guidance to the Drug Industry: Increased resources from user fees have enabled FDA to provide a large body of technical guidance to industry that clarifies the drug development pathway for many diseases. The resources also allow FDA to meet with companies during drug development to provide critical advice on specific development programs. During the past five years alone, FDA has held more than 7,000 meetings soon after we received a request from the product sponsors. Innovations in drug development are being advanced by many new companies as well as more established ones, and new sponsors may need, and often seek, more regulatory guidance during development. In FY 2009, more than half of the meetings FDA held with companies at the early investigational stage and midway through the clinical trial process were with companies that had no approved product on the U.S. market.

Weighing Drug Benefit and Risk: FDA assesses benefit-risk for new drugs on a case-by-case basis, considering the degree of unmet medical need and the severity and morbidity of the condition the drug is intended to treat. This approach has been critical to increasing patient access to new drugs for cancer and rare and other serious diseases, where existing therapies have been few and may have limited effectiveness. Some of these products have serious side effects but they were approved because the benefit outweighed the risk.

For example, in March of last year, FDA approved Yervoy (ipilimumab) for the treatment of unresectable or metastatic melanoma. Yervoy also poses a risk of serious side effects in 12.9 percent of patients treated, including severe to fatal autoimmune reactions. However, FDA decided that the benefits of Yervoy outweighed its risks, especially considering that no other melanoma treatment has been shown to prolong a patient's life.

FY 2013 User Fee Increase for PDUFA V: The legislation that the Administration submitted to Congress to reauthorize PDUFA recommends \$713 million in PDUFA fees for FY 2013. The current law expires on September 30, 2012, and FDA is ready to work with Congress to ensure timely reauthorization of this vital program. To sustain and build on our record of accomplishments, reauthorization must occur seamlessly, without any gap between the expiration of the old law and the enactment of PDUFA V.

Specifics of PDUFA V: We are very pleased to report that the enhancements for PDUFA V address many of the top priorities identified by public stakeholders, the top concerns identified by industry, and the most important challenges identified within FDA. I will briefly summarize these enhancements for the subcommittee.

Enhancing Application Review – To foster greater efficiency in the review process for new, innovative products – new molecular entities (NMEs) and original biologics license applications (BLAs) – PDUFA V promotes enhanced communication and additional meetings with firms that sponsor these applications. To accommodate this increased interaction during review, the FDA review clock for this subset of applications would not start until the 60-day administrative filing review period ends.

Enhancing Regulatory Science & Expediting Drug Development – PDUFA V includes five enhancements to advance regulatory science and expedite drug development.

- **Innovation through Enhanced Communication** – Under PDUFA V, FDA will promote innovation through enhanced communication between FDA and sponsors during drug development.
- **Methods for Meta-Analysis** – FDA will evaluate best practices for and the limitations of meta-analysis, a valuable form of statistical analysis that combines data or findings from multiple studies to explore drug benefits and risks.
- **Biomarkers and Pharmacogenomics** – FDA will augment its clinical, clinical pharmacology and statistical capacity to adequately address applications that rely on biomarkers.
- **Use of Patient-reported Outcomes** – FDA will improve its clinical and statistical capacity to address applications that include study outcomes known as patient-reported-outcomes and other clinical endpoint assessment tools.
- **Drugs for Rare Diseases** – FDA will foster the development of drugs for rare diseases by issuing guidance, increasing FDA outreach to the rare disease patient community, and providing specialized training in rare disease drug development for sponsors and FDA staff.

Enhancing Benefit-Risk Assessment – FDA will hold public workshops to discuss frameworks for evaluating benefits and risks that are most appropriate for drug and biological review. FDA will also conduct a series of public meetings between its review divisions and patient advocacy communities to receive their input on the severity of condition and degree of unmet medical need for specific indications or disease states.

Enhancing and Modernizing the FDA Drug Safety System – PDUFA V includes two important post-market, safety-focused initiatives. Under the first, standardizing Risk Evaluation and Mitigation Strategies (REMS), FDA will initiate a public process to explore strategies and initiate projects to standardize

REMS with the goal of reducing burden on practitioners, patients, and others in the health care setting. FDA will also conduct public workshops and develop guidance on methods for assessing the effectiveness of REMS and the impact on patient access and burden on the health care system. Under the second, evaluating drug safety issues through the Sentinel Initiative, FDA will initiate a series of projects to establish the use of active post-market drug safety surveillance to evaluate post-market safety signals in population-based databases.

Electronic Submissions and Standardization of Electronic Application Data –

The predictability of the FDA review process relies heavily on the quality of sponsor submissions. FDA currently receives submissions of original applications and supplements in formats ranging from paper-only to electronic-only, as well as hybrids of the two. The variability and unpredictability of submitted formats and clinical data layout present major obstacles to conducting a timely, efficient, and rigorous review within current PDUFA goal time frames. PDUFA V enhancements include a phased-in requirement for standardized, fully electronic submissions for all marketing and investigational applications. Through partnership with open standards development organizations, FDA will also conduct a public process to develop standardized terminology for clinical and non-clinical data submitted in marketing and investigational applications.

B. Medical Device User Fees

Introduction: Action by Congress in 2002 to enact the Medical Device User Fee and Modernization Act (MDUFMA I) was prompted by growing concerns about the capacity and performance of the medical device review program. MDUFMA I and MDUFA II (enacted in 2007) authorized user fees for the review of medical device premarket applications, reports, supplements, and premarket notification submissions. The additional resources generated by MDUFA fees allowed FDA to make its reviews more timely, predictable, and transparent to applicants. MDUFA fees and other appropriations for the medical device program helped FDA expand available expertise, modernize its information management systems, provide new review options, and provide more guidance to prospective applicants.

MDUFA II Performance: FDA has been meeting or exceeding goals agreed to by FDA and industry under MDUFA II for most of the submissions that FDA reviews each year. For example, FDA completes at least 90 percent of 510(k) reviews within 90 days or less.

FDA's performance during MDUFA II has not been limited to achieving quantitative goals for the timely review of premarket submissions such as applications for Premarket Approval (PMAs) and requests for 510(k) clearance. FDA also accomplished a number of qualitative goals set by MDUFA II in 2007, including issuing more than 50 new and updated guidances for industry. Guidance documents are important resources for industry because they describe FDA's interpretation of or policy on regulatory issues. Guidances are critical to support industry efforts to comply with the law and to develop new products that may benefit American patients. The availability of guidance documents also fosters regulatory predictability and consistency.

It is important to note that MDUFA metrics reflect FDA time only. The metrics do not reflect the time taken by device sponsors to respond to requests for additional information. Overall time to decision – the time that FDA has the application plus the time the manufacturer spends answering any questions FDA may have – has increased steadily since 2001.

FDA bears some responsibility for the increase in total time to decision, and we have been instituting management, policy, and process changes to address this issue. As a result, in 2011, FDA for the first time began reducing what previously was an increasing backlog of unresolved 510(k) submissions.

Smart Regulation and Fostering Medical Device Innovation: FDA recognizes that, if the United States is to maintain its leadership role in this area we must continue to streamline and modernize processes and procedures to make device approval not just scientifically rigorous, but clear, consistent, and predictable without compromising safety. FDA is committed to continuing to improve the device approval process to address legitimate concerns raised by industry and other stakeholders.

Nearly two years ago, FDA recognized that, given the growing complexities of medical product development, FDA needed to re-evaluate and modernize regulatory review processes to ensure that patients had timely access to safe and effective medical devices. At that time, CDRH began a new, systematic approach to device regulation, moving away from the traditional misperception that safety and effectiveness considerations are incompatible with fostering innovation. Rather than focus on more regulation or less regulation, we began to focus on smart regulation.

The new approach is to ensure that safety and effectiveness and innovation are complementary, mutually supporting aspects of FDA's mission to promote public health. To improve CDRH's internal systems, we first reached out to stakeholders to hear their concerns and listen to their recommendations about premarket programs. This is what we heard:

- Industry felt that inadequate predictability, consistency, and transparency were stifling innovation and driving jobs overseas.
- Consumer groups, third-party payers, and some health care professionals believed that one of the premarket pathways – the 510(k) program – did not provide adequate protection for American patients and did not generate sufficient information for practitioners and patients to make well-informed treatment and diagnostic decisions.

In turn, CDRH employees expressed concerns that the 510(k) program had not adapted to the increasing complexity of devices, and that poor-quality 510(k) submissions, poor-quality clinical studies conducted in support of PMA applications, and an ever-growing workload were straining already overburdened premarket programs.

FDA also began two assessments of device premarket programs to identify issues, their root causes, and the appropriate solutions. One assessment focused on the 510(k) program. The other examined how FDA uses science in regulatory decision-making, touching on aspects of several of the device premarket review pathways, such as our clinical trials program. In addition, FDA contracted with the Institute of Medicine (IOM) to conduct an independent evaluation of the medical device 510(k) program.

In August 2010, following extensive public input, FDA released two reports that identified issues regarding the medical device premarket programs and proposed potential actions to address the underlying root causes. The number one problem was insufficient predictability in device premarket programs, which can create inefficiencies, increase costs for industry and FDA, and delay bringing safe and effective products to market. We identified several root causes of these issues. They include:

- very high reviewer and manager turnover at CDRH (almost double that of FDA's drug and biologics centers)
- insufficient training for staff and industry
- extremely high ratios of employees to front-line supervisors
- insufficient oversight by managers
- CDRH's rapidly growing workload, caused by the increasing complexity of devices and the number of overall submissions we review
- unnecessary or inconsistent data requirements imposed on device sponsors
- insufficient guidance for industry and FDA staff
- and poor-quality submissions from industry.

While it is true that providing more user fee resources alone will not solve the problems of the device premarket programs, funding needs is the root of, or a contributing factor to, several of these problems. Adequate and stable funding is one key component to FDA and industry success in bringing safe and effective devices to market quickly and efficiently.

After considering extensive and varied public input on our recommendations, in January 2011, FDA announced a Plan of Action that included 25 specific actions that we would take in 2011 to improve the predictability, consistency, and transparency of device premarket programs. As of February 2012, 75 percent of these actions, plus eight additional actions, are already completed or well underway.

In addition, during February 2011, FDA announced the Innovation Initiative, which included several proposals to help maintain the position of the U.S. as the world's leader in medical device innovation, including the creation of a new approach for important, new technologies called the Innovation Pathway.

Since then, FDA has announced additional efforts to improve medical device premarket programs, including actions to improve the program for clinical trials and the Investigational Device Exemption (IDE) program. The actions we are taking can be grouped into three main areas of emphasis. Overall, FDA actions seek to:

- create a culture change toward greater transparency, interaction, collaboration, and the appropriate balancing of benefits and risks
- ensure more predictable and consistent recommendations, decision-making, and application of the least-burdensome principle
- implement more efficient processes and use of resources.

FDA believes the actions that we've taken and plan to take in the future will have a positive impact on the device review process by

- providing greater predictability of data requirements through guidance
- reducing unnecessary data requests through training and policy and process changes
- implementing policies to appropriately balance benefit-risk determinations
- using external experts more extensively (consistent with conflict-of-interest guidelines)
- creating incentives to conduct clinical studies first in the United States
- speeding up IDE approval decisions
- implementing the Innovation Pathway 2.0 (a priority review program to expedite development, assessment, and review of important technologies)
- instituting efficiencies in the premarket review process.

To best serve patients, both the medical device industry and FDA must have the flexibility to be innovative and entrepreneurial. CDRH must continue making critical improvements to the device program. At the same time, the medical device industry and CDRH must continue to work together to ensure that the Center receives high-quality submissions that contain the information we need to make well-informed and timely decisions.

Finally, CDRH must have adequate and stable resources to get the job done right and quickly. Timely reauthorization of MDUFA, as well as the Congressional appropriations process, is critical to achieving these goals.

Moving Forward – Reauthorization of MDUFA: For more than a year, FDA has been meeting with stakeholders and holding discussions with the medical device industry in an effort to develop a package of recommendations to reauthorize MDUFA. On February 1, we reached an agreement in principle with representatives from the medical device

industry on a set of recommendations to reauthorize MDUFA. The agreement would authorize FDA to collect \$595 million in user fees over five years, an amount that is subject to inflation increases. The President's Budget for FY 2013 recommends a MDUFA fee amount of 69.7 million. As the MDUFA III agreement moves forward, we will update this amount to reflect the new funding levels for FY 2013. The agreement strikes a careful balance between what industry agreed to pay and what FDA can accomplish with the proposed funding. We believe that it will result in greater predictability, consistency, and transparency through improvements to the review process.

Key features of the agreement include the following:

- Earlier, more transparent and more predictable interactions between FDA and applicants, both during the early product development stage as well as during the review process
- More detailed and objective criteria for determining when a premarket submission is incomplete and should not be accepted for review
- More streamlined FDA review goals that will provide better overall performance and greater predictability. This includes a commitment to provide feedback to an applicant if FDA's review extends beyond the goal date, so that the parties can discuss how to resolve any outstanding issues
- Additional resources to support guidance development, reviewer training and professional development, and an independent assessment of the pre-market review process to identify potential enhancements to efficiency and effectiveness
- More detailed quarterly and annual reporting of program performance
- A commitment between FDA and industry to reduce the total average calendar time to a decision for PMAs and 510k applications.

FDA and representatives of the medical device industry recently completed negotiating the final details of the agreement, and the Administration is reviewing the draft package of proposed recommendations. When this review is completed, FDA will present that package to Congressional committees and will seek public comment on the proposed recommendations, which will include a public meeting. FDA will then consider the public's views and comments, revise the proposed recommendations as necessary, and transmit final MDUFA reauthorization recommendations to Congress.

As we work with all interested stakeholders and Congress toward reauthorization of MDUFA in order to provide adequate and stable funding for the program, we will also be moving forward with the ongoing CDRH program improvements, focusing on smart regulation that will facilitate device innovation. As these new policies and processes continue to be implemented, we expect to see notable improvements in the consistency, transparency, and predictability of the medical device premarket review programs.

C. Tobacco Product User Fees

On June 22, 2009, President Obama signed the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act) into law. This legislation granted FDA authority to regulate the manufacture, marketing, and distribution of tobacco products, and it authorized the agency to collect user fees from manufacturers and importers of tobacco products to pay for new FDA tobacco regulation activities. The legislation specified the total dollar amount to be collected each year, and directed the manner in which the fees would be assessed among classes of tobacco products, and among companies within each class.

Since 2009, FDA successfully has stood up the Center for Tobacco Products (CTP). CTP has used the user fees prescribed in the statute to hire Center leadership and to enable those leaders to initiate the scientific, educational, enforcement and regulatory activities needed to accomplish the public health goals of the Tobacco Control Act. By the end of FY 2011, the Center had a staffing level of over 230 FTEs, and it anticipates meeting projected staffing goals in FY 2013.

Importantly, since 2009, CTP already has advanced the public health significantly by:

- Enforcing a ban on cigarettes with characterizing flavors, other than menthol, such as cherry and chocolate;
- Issuing and enforcing regulations that restrict youth access to cigarettes and smokeless tobacco;
- Enforcing the prohibition on misleading advertising claims, including those that misleadingly imply products are safer;
- Enforcing requirements for the new smokeless tobacco warnings that better communicate health risks; and
- Issuing new cigarette health warnings that will promote better understanding of the dangers of smoking.

In addition, CTP has:

- Established a world-class testing laboratory with expertise and capacity to analyze tobacco products and increase our understanding the health risks of these products.
- Supported innovative research on the impact of altering nicotine levels in tobacco products to assess how such changes could affect the way people might use tobacco products.

- Dramatically increased regulatory science capabilities, along with the National Institutes of Health, via the launch of the first-ever sustained, longitudinal study to understand patterns of tobacco use and how it changes over time in youth and adults, including vulnerable populations.
- Protected millions of youth by awarding nearly \$33 million to 37 states and the District of Columbia for conducting retail inspections to ensure that tobacco retailers comply with the law's requirements, such as not selling cigarettes and smokeless tobacco products to minors.
- Conducted more than 40,000 retail inspections under these State contracts, resulting in over 2,000 warning letters for violations. Further, FDA has started issuing Civil Money Penalties for continued violations; and
- Issued guidance to industry to help them meet their obligations under the law with respect to substantial equivalence and new tobacco product applications.

The FY 2013 budget request for CTP is \$505,000,000, an increase of \$28,000,000 above the FY 2012 enacted budget. The amount requested is specifically authorized in the Tobacco Control Act and comprised entirely of tobacco user fees. FY 2013 priorities include strong measures to prevent youth from starting to use tobacco, reduce product harms, and encourage current users to quit.

In an effort to prevent youth from starting to use tobacco products (*i.e.*, initiation), CTP plans to:

- Deem all products that meet the definition of tobacco product to be subject to FDA's tobacco product authorities;
- Launch a series of comprehensive, science-based public education campaigns, targeting youth and young adults, to educate about the dangers of tobacco products; and
- Continue to expand the State Retail Enforcement Program, awarding additional contracts toward the goal of contracting with every state and U.S. territory to assist with FDA tobacco retail inspections.

In an effort to reduce harm from tobacco products, CTP plans to:

- Enact a new rule that requires testing and reporting to FDA about harmful and potentially harmful constituents and subsequently use the data to educate the public about the health risks of these constituents;
- Continue research to support development of tobacco product standards to reduce the addictiveness of current products; and

- Continue research to support the development of tobacco product standards to reduce toxic, cancer-causing elements in tobacco products and tobacco smoke.

Finally, in an effort to encourage tobacco users to quit, CTP plans to work to ensure that tobacco product marketing is neither false nor misleading.

D. New User Fees for Generics and Biosimilars

In addition to recommending the reauthorization of PDUFA and MDUFA, the FY 2013 Budget recommends new user fee programs to support review and related activities for generic drugs and biosimilars. The proposed user fee programs for generic drugs and biosimilars are modeled on the successful PDUFA program but are tailored to reflect the unique challenges and needs associated with regulating generic drugs and biosimilars.

1. Generic Drug User Fees

As a result of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Amendments, America's generic drug industry has been developing, manufacturing, and marketing – and FDA has been reviewing and approving – lower-cost versions of brand-name drugs for more than 25 years. This legislation and the industry it fostered are a true public health success.

Last year, approximately 78 percent of the more than three billion new and refilled prescriptions dispensed in the United States were filled with generics, yet those drugs accounted for only 25 percent of prescription drug spending. In the last decade alone, generic drugs have provided more than \$931 billion in savings to the nation's health care system.

This success, however, also has come to represent a significant regulatory challenge, and delays in approvals of generic drugs have emerged as a major concern for the generics industry, FDA, consumers, and payers alike. Unlike the brand manufacturers who pay fees under PDUFA, the generic industry does not currently pay a user fee to support FDA activities related to its applications. During the past several years, despite actions by this Subcommittee to increase funding for generic drugs, FDA resources have not kept pace with the ever increasing number of Abbreviated New Drug Applications (ANDA) and other submissions related to generic drugs.

The number of generic drug submissions sent annually to FDA has grown rapidly, reaching another record high this year, including nearly 1,000 ANDAs. The current backlog of pending applications is estimated to be more than 2,500. The current median time to approval is approximately 31 months, although this includes time that the application is with the sponsor to address FDA questions about the application.

The regulatory challenge of ensuring safe, high-quality generic drugs includes inspecting manufacturing facilities, where the challenge is not just one of numbers but also of geography. To keep pace with the growth of the generic drug industry, FDA has had to

conduct more inspections as the number of facilities supporting those applications has also increased, with the greatest increase coming from foreign facilities, including those that manufacture Active Pharmaceutical Ingredients (APIs) and Finished Dosage Forms (FDFs).

The number of foreign manufacturers greatly exceeds the number found in the United States, and both API and FDF manufacturers must be inspected for FDA to approve a generic drug application. The generic industry is also experiencing significant growth in India and China, a trend that will likely continue. Foreign inspections represent a significant challenge and require significant resources.

The generic drug user fee agreement is designed to address these regulatory challenges in an affordable manner. The annual fee total proposed represents less than one half of 1 percent of generic drug sales. This modest cost is expected to be offset by benefits received by the industry, as faster review times will bring products to market sooner. The result will also be more savings for patients, health care systems, and the government.

Overview of the Proposed Generic Drug User Fee Proposal: The Generic Drug User Fee Act (GDUFA) proposal submitted to Congress in January 2012 is aimed at putting FDA's generic drugs program on a firm financial footing and providing the additional resources necessary to ensure timely access to safe, high-quality, affordable generic drugs. With the proposed user fee resources, FDA will enhance the generic drug review process and increase FDA's capacity to conduct reviews of Abbreviated New Drug Applications (ANDAs) and associated Drug Master Files (DMFs) with greater efficiency and transparency. FDA will conduct additional pre-approval, bioequivalence, and post-market surveillance inspections to verify manufacturing compliance with Current Good Manufacturing Practices (CGMP) for generic drug products. The FY 2013 user fee estimate for GDUFA is \$299 million.

The proposal focuses on quality, access, and transparency. Quality means ensuring that companies, foreign or domestic, that participate in the U.S. generic drug system are held to the same consistent high-quality standards and that their facilities are inspected biennially, using a risk-based approach, with foreign and domestic inspection frequency parity.

Access means expediting the availability of low-cost, high-quality generic drugs by bringing greater predictability and timeliness to the review of ANDAs, amendments, and supplements. Transparency means requiring the identification of facilities involved in the manufacture of generic drugs and associated APIs, and improving FDA's communications and feedback with industry to expedite product access and enhance FDA's ability to protect Americans in our complex global supply environment.

The additional resources called for under the agreement will provide FDA with the ability to perform critical program functions that could not otherwise occur. With the adoption of user fees and the associated savings in development time, the overall expense of bringing a generic product to market is expected to decline. The program is expected to provide significant value to small companies and first-time entrants to the generic market.

In particular, these companies will benefit significantly from the certainty associated with performance review metrics that offer the potential to dramatically reduce the time needed to commercialize a generic drug, when compared to pre-GDUFA review times.

GDUFA Program Funding and Metrics: If enacted as negotiated, the program would provide FDA with additional funding for all aspects of the generic drug program in the amount of \$299 million per year, for five years, adjusted annually for inflation. With those additional user fee funds, FDA agrees to undertake a series of immediate program enhancements and performance goals. Many performance metrics and efficiency enhancements are set forth in the negotiated documents. The proposed goals, many of which will be phased in, include:

- **New Applications:** FDA will review and act on 90 percent of complete, unamended electronic ANDAs within 10 months after the date of submission.
- **Backlog:** FDA will review and act on 90 percent of all ANDAs, ANDA amendments, and ANDA prior-approval supplements pending on October 1, 2012, by the end of FY 2017.
- **Inspections:** FDA will conduct risk-adjusted biennial Current Good Manufacturing Practice (CGMP) inspections of generic API and generic FDF manufacturers with the goal of achieving parity of inspection frequency between foreign and domestic firms in FY 2017.

Under the program, fees will derive from two primary sources: generic drug-related submissions and generic drug-related facilities. In the first year of the program, there would also be a fee assessed for applications that are pending on October 1, 2012, the so-called “backlog.”

Like PDUFA, individual fee amounts would be set annually, with the total annual user fee revenue target specified in statute. Overall, 70 percent of the user fee revenue will be generated by facility fees and 30 percent by ANDA application, prior approval supplement and Drug Master File fees. In the first year that ratio will be slightly different because of the one-time backlog fee. The revenue from facilities is split, with 80 percent provided by the FDF manufacturers and 20 percent by API manufacturers, a ratio recommended by the generics industry.

As in all of FDA’s other medical product user fee programs, under the proposed generic drug user fee program, user fee funding will supplement appropriated funding to ensure sufficient resources for FDA’s generic drug review program, and guarantees are in place to ensure that the user fees supplement annual appropriations.

2. Biosimilars User Fees

A successful biosimilars review program within FDA will spark the development of a new segment of the biotechnology industry in the United States. The Biologics Price Competition and Innovation Act (BPCI Act) of 2009 established a new abbreviated

approval pathway for biological products shown to be “biosimilar to” or shown to be “interchangeable with” an FDA-licensed biological product. With this new abbreviated approval pathway, a biosimilar biologic can be approved by demonstrating, among other things, that it is highly similar to a reference biological product already licensed by FDA.

Developing a biosimilar is expected to be less risky, less costly, and less time-consuming than developing the reference biological product manufactured by an innovator company. Therefore, approved biosimilars are expected to be less expensive. This program will provide significant benefits for patients, making available more affordable treatments that clinicians will know that are biosimilar or that are interchangeable. The development of this new market segment will expand the opportunities for technical innovation and job growth.

Biosimilar Fee Program Funding and Metrics: The FY 2013 estimate for biosimilar user fees is \$20.2 million. The proposed biosimilars user fee program for FY 2013 to 2017 addresses many of the top priorities identified by public and industry stakeholders and the most important challenges identified by FDA. The proposed biosimilars user fee program is similar to the PDUFA program in that it includes fees for marketing applications, manufacturing establishments, and products. However, there are some differences, because of the nascent state of the biosimilars industry in the United States. For example, there are no currently marketed biosimilar biological products. Accordingly, the recommended biosimilars user fee program includes fees for products in the development phase. This program will generate fee revenue in the near-term and enable sponsors to have meetings with FDA early in the process of developing biosimilar biological product candidates.

As in all of FDA’s medical product user fee programs, the proposed biosimilars user fee program supplements appropriated funding to ensure sufficient resources for FDA’s review programs. Under the proposed biosimilars user fee program, FDA would be authorized to spend biosimilars user fees on FDA activities related to the review of submissions in connection with biosimilar biological product development, biosimilar biological product applications, and supplements. This program would include activities related to biosimilar biological product development meetings and investigational new drug applications (INDs). It would also include development of the scientific, regulatory, and policy infrastructure necessary for review of biosimilar biological product applications, such as regulation and policy development related to the review of biosimilar biological product applications, and development of standards for biological products subject to review and evaluation.

Details of Proposed Biosimilar Fees: The proposed biosimilars user fee program includes biosimilar product development, marketing application, establishment, and product fees.

The initial and annual biosimilar product development fees for biosimilar biological products in development would be equal to ten percent of the fee established for a human drug application under PDUFA for that fiscal year. The sponsor would pay biosimilar product development fees each year until the sponsor submits a marketing application for

the product that is accepted for filing or discontinues participation in the biosimilar product development program for the product. The proposed marketing application fee for a biosimilar biological product is equal to the fee established for a human drug application under PDUFA, minus the cumulative amount of any biosimilar product development fees paid for the product that is the subject of the application.

Finally, the proposed establishment and product fees are equal to the establishment and product fees under PDUFA for any fiscal year because the level of effort required for FDA oversight of manufacturing and post-marketing safety activities is expected to be comparable for biosimilars and biological products under PDUFA. FDA anticipates a modest level of funding from these sources initially, because only biosimilar biological products that are approved for marketing would be subject to these fees.

Proposed Biosimilar Performance Goals and Procedures: The proposed performance goals for biosimilars are similar to the PDUFA performance goals. They include performance goals for application review, first-cycle review, proprietary name review, major dispute resolution, clinical holds, and special protocol assessments. The proposal also includes goals for new types of development-phase meetings with associated time frames for timely review of data and feedback.

E. Implementing the FDA Food Safety Modernization Act

Food Safety remains a critical program area for FDA. FDA's FY 2013 proposal for food safety aims to advance the vision of a strong, reliable food safety system that Congress enacted in the landmark FDA Food Safety Modernization Act of 2011 (FSMA). The FY2013 budget proposal builds on the food safety increases that the subcommittee appropriated for FY 2011 and FY 2012, and calls for novel user fee revenue to allow FDA to establish a prevention-focused domestic and import food safety system. (These efforts will include leveraging the valuable work of FDA's food safety partners in foreign state, local, tribal, and territorial governments.)

Congress' Vision for FSMA: Passed in response to a series of outbreaks and contamination incidents involving both domestic and imported food that revealed serious weaknesses in the nation's system of food protection, FSMA set out a vision for a modern food safety system that shifts the focus to preventing food safety problems rather than relying primarily on reacting to problems after they occur. It was enacted with broad consumer and industry support and reflects a shared vision that all Americans will benefit from a modernized food safety system that reduces foodborne illness, strengthens public confidence in food safety, and minimizes costly disruptions of the food supply.

Implementing Congress' vision for a strengthened food safety system represents a dramatic expansion of FDA's workload. The statute calls for: food safety standards for produce; comprehensive implementation of preventive controls across all food and feed facilities; new inspection frequency mandates for food facilities; an entirely new import oversight system and mandated presence overseas; and a mandate to build capacity of states and foreign government to achieve harmonization and leverage resources. These

elements are visionary, but the simple truth is that FDA cannot meaningfully deliver on these mandates without sufficient funding.

FDA is redeploying current resources and pursuing efficiencies to implement FSMA, but in a constrained budget environment, it is appropriate for industries that directly benefit from FDA activities to pay moderate fees to fund some of FDA's critical new responsibilities enacted in FSMA. We look forward to working with Congress to ensure that there are sufficient and appropriate user fee resources for FDA to implement the requirements of the Food Safety Modernization Act.

FSMA's direction to FDA – essentially to build a modern new food safety system that can work more effectively to prevent food safety problems and meet the challenges of today's global food system – reflects a recognition of the food safety realities in America, including the rising volume of food imports and the high costs of foodborne illness.

The Rising Volume of Food Imports: The statistics on our food supply provide some insight into what prompted Congress to act. On the rising volume of food imports, FDA regulates more than \$450 billion of domestic and imported foods. An estimated 15 percent of the U.S. food supply is imported, including 50 percent of fresh fruits, 20 percent of fresh vegetables, and 80 percent of seafood. These imports originate from more than 250,000 foreign establishments in 200 countries each year. As a nation, we enjoy the benefits of – but are simultaneously put at risk by -- a global food supply.

The Cost of Foodborne Illness: In addition to the globalization challenge, the costs of foodborne illness are significant: Outbreaks caused by contamination in the food and feed supply impose costs on consumers, the food and feed industries, and the health care system. A 2012 study using an enhanced cost-of-illness model estimated that the aggregated cost of foodborne illness is \$77.7 billion per year. The average cost per case of foodborne illness is \$1,626. Outbreaks of foodborne illness and contamination events have a substantial impact on public health – 48 million foodborne illnesses occur every year resulting in 128,000 hospitalizations and 3,000 deaths.

In June 2011, the U.S. Department of Agriculture (USDA) Economic Research Service (ERS) estimated that the annual economic cost of foodborne illness and premature death caused by Salmonella is \$2.7 billion. The annual estimated cost of illness caused by E. coli O157 is \$489 million. These estimates include medical costs due to illness, the cost of time lost from work due to nonfatal illness, and the cost of premature death. Reducing foodborne illness by just 10 percent would keep 5 million Americans from getting sick each year. Preventing a single fatal case of E. coli O157 infection would save an estimated \$7 million.

Strategic Plan: As the subcommittee directed in the conference agreement to accompany our FY 2012 appropriation, FDA has issued a strategic plan for food safety. Known as the Food and Veterinary Medicine Strategic Plan, this plan contains FDA's strategy for food safety and preventing foodborne illness. The plan targets foodborne illnesses of unknown origins as well as illness that can be specifically attributed to known sources.

The Food and Veterinary Medicine Strategic Plan is based on goals including:

- Improving food safety effectiveness and efficiency at all levels of the food and feed supply chain
- Establishing science-based preventive control standards across the farm-to-table continuum;
- Achieving high rates of compliance with preventive controls standards domestically and internationally; and
- Strengthening scientific leadership, capacity, and partnership to support public health and animal health food safety decision making.

FY 2013 Food Establishment Registration Fee: To address the challenges of globalization and the high costs of foodborne illness, to implement FSMA, and to advance the goals of the Food and Veterinary Medicine Strategic Plan, FDA is proposing a new food facility registration user fee of \$220.2 million for FY 2013. The fee will support:

- establishing new, effective, and comprehensive food safety standards
- establishing a new program for import safety
- increasing the number and efficiency of inspections
- launching an integrated national food safety system with states and localities
- expanding research activities, which will include improved data collection and risk analysis
- improving FDA's capability to conduct risk-based decision-making.

These fees will allow FDA to reduce the risk of illness associated with food and feed, decrease the frequency and severity of food- and feed-borne illness outbreaks, reduce instances of contamination; and greatly diminish the burden on American businesses and the U.S. economy due to foodborne illness events. Without sufficient and reliable fee revenue, we can expect the unacceptably high human toll of foodborne illness to continue, with the resulting disruptions to the food system and the economic burdens to the food industry that result from foodborne illness outbreaks.

Fee revenue would provide a modest share of total resources required for FSMA implementation and FDA's other food safety activities, but is essential to meet the statutory mandates; enable investments in training, IT, and other areas that will enhance FDA's efficiency; and secure FDA's base funding. These proposed user fee investments are quite modest compared to the economic value of the nation's food and feed supplies

and the costs that the public, industry, government, and the health care system experience during an outbreak. FDA is engaging with the food industry and other food safety stakeholders to develop a workable fee structure that will have broad support within the food industry, other stakeholders and Congress.

Major Pathogens Responsible for Foodborne Illness: Finally, the conference agreement on the FY 2012 budget also directed FDA to link its budget request for food safety to actions that will attack the known and the unknown sources of foodborne illness. FDA has embraced this approach across all components of the FY 2013 budget relating to food safety – the FDA business case papers, performance tables, and center-by-center narratives. Specifically, the FY 2013 budget includes more than 125 references to the top seven causes of foodborne illness.

F. Other New User Fee Proposals

Cosmetics User Fee: The proposed cosmetic user fee of \$18.7 million will strengthen FDA efforts to protect public health by preventing harm to consumers, ensuring the safety of cosmetics and removing unsafe cosmetics from the market. With this fee revenue, FDA will develop necessary guidance and standards for industry. The fee revenue will also allow FDA to identify research gaps, such as gaps related to the safety of novel ingredients used in cosmetics.

Medical Product Reinspection User Fee: The FDA Food Safety Modernization Act, which Congress enacted in December 2010, authorized fees for reinspections of food and feed establishments. FDA is proposing to expand this fee authority to medical product establishments. With this change, medical product establishments will pay the full cost of reinspections and associated follow-up work. FDA will impose the user fee when FDA reinspects facilities due to a failure to meet Good Manufacturing Practices (GMPs) or other important FDA requirements. The FY 2013 estimate for Medical Product Reinspection user fees is \$14.7 million.

Food Contact Notification User Fee: FDA has statutory responsibility for the safety of all food contact substances in the United States. The Food Contact Notification (FCN) program supports applications for innovative food contact substances that help mitigate microbial food contamination and provide consumers with more healthful and safe food choices. The proposed user fees of \$4.9 million will support FDA efforts to increase the availability of safe food contact substances, to prevent unsafe food contact substances from reaching the market and to apply the most modern regulatory science to the review of food contact substances.

International Courier Use Fee: For FY 2013, FDA is proposing a new International Courier User Fee of \$5.6 million. The proposed fee will support activities associated with increased surveillance of FDA-regulated commodities at express courier hubs. To address the growing volume of imports entering through international couriers, FDA is proposing to pay the increased cost of its international courier activities through user fees.

CONCLUSION: THE PROMISE AND THE CHALLENGE

The resources in this budget will allow FDA to perform its fundamental public health responsibilities in new and more efficient ways. Our budget also supports industry efforts to innovate and bring new products to market that will benefit American patients and consumers and strengthen our economy.

It is fitting that that today is International Rare Disease Day. The difficulties in promoting the development of safe and effective therapies for diseases afflicting small populations highlights both the accomplishments we are now delivering to the American people and the public health challenges facing FDA.

Rare diseases often appear early in life, and about 30 percent of children with rare diseases die before the age of 5. By some estimates, there are 7,000 rare diseases afflicting about 25 million Americans. For these Americans, today – and every day – is Rare Disease Day.

Because of the small numbers of patients who suffer from each disease, FDA often allows drug sponsors to use non-traditional approaches to establishing safety and effectiveness. For example, FDA approved Voraxaze (glucarpidase) just last month, to treat patients with toxic methotrexate levels in their blood due to kidney failure. Voraxaze was approved based on data in 22 patients from a single clinical trial. Prior to the approval of Voraxaze, there were no effective therapies for the treatment of toxic methotrexate levels in patients with renal failure.

Similarly, less than a month ago, FDA approved Kalydeco (ivacaftor) to treat patients age 6 or older with Cystic Fibrosis (CF) and who have a specific genetic defect (G551D mutation). The G551D mutation occurs in approximately 4 percent of patients with CF, or approximately 1,200 patients in the United States. There is no cure for CF, and despite progress in the treatment of the disease, most patients with CF do not live beyond their mid-30's. FDA granted Ivacaftor Priority Review status, and approved the drug in approximately half of the six-month Priority Review period. Ivacaftor will be the first medicine that targets the underlying cause of CF.

Although these successes are encouraging, much work remains. Less than five percent of the 7,000 orphan diseases are treatable today. We recognize our vital role in bringing new therapies and new hope to patients who suffer from rare diseases, which is why FDA made drugs to treat rare diseases one of our priorities for the reauthorization of the Prescription Drug User Fee Act.

Much work remains ... not just for orphan drugs, but for all FDA-regulated products. The challenges of promoting innovation while assuring safety will only increase in the coming years, along with exciting opportunities to improve public health through new cures and a safer food supply.

My goal with this proposed FY 2013 budget is to position FDA to seize these opportunities. The resources in this budget will allow FDA to perform its core public health responsibilities in new and more efficient ways, to address these and the many other challenges at the heart of our mission. This budget also supports industry efforts to innovate and bring new products to market that will benefit American patients and consumers and strengthen our economy.

Thank you for the opportunity to testify. I am happy to answer your questions.