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FOOD AND DRUG ADMINISTRATION AMENDMENTS ACT OF 2007

JULY 11, 2007.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

Mr. DINGELL, from the Committee on Energy and Commerce, submitted the following

R E P O R T

together with

ADDITIONAL VIEWS

[To accompany H.R. 2900]

[Including cost estimate of the Congressional Budget Office]

The Committee on Energy and Commerce, to whom was referred the bill (H.R. 2900) to amend the Federal Food, Drug, and Cosmetic Act to revise and extend the user-fee programs for prescription drugs and for medical devices, to enhance the postmarket authorities of the Food and Drug Administration with respect to the safety of drugs, and for other purposes, having considered the same, report favorably thereon without amendment and recommend that the bill do pass.

CONTENTS

	Page
Purpose and Summary	2
Background and Need for Legislation	5
Hearings	13
Subcommittee Consideration	14
Committee Consideration	15
Committee Votes	15
Committee Oversight Findings	18
Statement of General Performance Goals and Objectives	18
New Budget Authority, Entitlement Authority, and Tax Expenditures	18
Earmarks and Tax and Tariff Benefits	18
Committee Cost Estimate	18
Congressional Budget Office Estimate	18

59–006

Federal Mandates Statement 25
Advisory Committee Statement 25
Constitutional Authority Statement 25
Applicability to Legislative Branch 25
Section-by-Section Analysis of the Legislation 25
Changes in Existing Law Made by the Bill, as Reported 64
Additional Views 196

PURPOSE AND SUMMARY

The bill, H.R. 2900, consists of nine titles.

TITLE I. PRESCRIPTION DRUG USER FEE AMENDMENTS OF 2007

Title I reauthorizes the prescription drug user fee program through fiscal year 2012. Changes to the prescription drug user fee program fall into three major categories: enhancements to ensure sound financial footing for the human drug review program, enhancements for premarket review of human drug applications, and enhancements to modernize and transform the postmarket safety system.

Title I includes the Administration's request for an increase in the total annual user fees collected to $392.8 million for FY2008, an $87.4 million increase over the current base. The increases in fees take into account inflation and increased resources needed to conduct certain activities, known as a workload adjustment. Title I also expands the amount and scope of fees devoted to postmarket safety. H.R. 2900 contains an additional $225 million in user fees that will be collected over five years. These additional funds are intended to be used for drug safety activities and are intended to supplement and not supplant any other drug safety resources. There will be a dollar-for-dollar decrease in user fees collected for these additional drug safety activities for every dollar appropriated for the same purpose.

Title I establishes a new program to assess, collect, and use fees for the voluntary review of prescription drug direct-to-consumer (DTC) television advertisements. This title also requires the Food and Drug Administration (FDA), and the drug companies and biotechnology firms that pay fees to FDA, to allow other stakeholders such as consumer and patient advocates to participate in the negotiations for PDUFA V.

TITLE II. MEDICAL DEVICE USER FEE AMENDMENTS OF 2007

Title II reauthorizes medical device user fees through FY2012. Changes to the medical device program fall into two major categories: enhancements to ensure sound financial footing for the device review program, and enhancements to the process for premarket review of device applications. Medical device companies will pay 31 percent more in fees in 2008 and 8.5 percent more in each subsequent fiscal year through 2012. This will ensure fee increases over the next five years to cover anticipated costs related to rent, security, and statutorily mandated payroll and benefit increases.

In an effort to add stability to this fee program, Title II includes two new types of fees that are intended to generate about 50 percent of the total fee revenue. The new fees are an annual establishment registration fee and an annual fee for filing periodic reports, for devices approved under a Premarket Approval Application (PMA), to FDA that provides, at least on an annual basis, a variety

of information, including manufacturing and design changes, and new studies involving their products. This title authorizes $7,100,000 in appropriations for additional postmarket safety activities. Title II also includes provisions to streamline the third-party inspection program.

Title II requires FDA, and the manufacturers of medical devices that pay fees to FDA, to allow other stakeholders such as consumer and patient advocates to participate in the negotiations for MDUFMA III.

TITLE III. PEDIATRIC MEDICAL DEVICE SAFETY AND IMPROVEMENT ACT

Title III provides incentives to device manufacturers to create medical devices specifically designed to meet the needs of pediatric patients. It also gives FDA the authority to review these devices in a manner distinct from devices in general, and to require postmarket studies to ensure the continued safety and effectiveness of these devices. The provisions of Title III only apply to devices that are used in 4,000 or fewer individuals.

Title III modifies the existing humanitarian device exemption (HDE) for medical devices to allow manufacturers of HDE-approved devices specifically designed to meet a pediatric need to make a profit from the sale of such devices. This HDE modification will sunset in 2013.

Title III authorizes FDA to establish a mechanism to track the number and types of devices approved specifically for children or for conditions that occur in children. Title III also grants explicit authority to FDA's Pediatric Advisory Committee to monitor the use of pediatric devices and to make recommendations for improving their availability and safety.

TITLE IV. PEDIATRIC RESEARCH EQUITY ACT OF 2007

Title IV reauthorizes FDA's authority to require a manufacturer of a drug or biologic who submits an application to market a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration to also submit a pediatric assessment.

Title IV grants the Secretary of the Department of Health and Human Services (HHS) permanent authority to require pediatric tests in appropriate circumstances. The title strengthens provisions of current law that allow a deferral of pediatric tests for new products. The standard requiring tests for drugs currently being marketed is also strengthened. Requirements with respect to labeling drugs are strengthened to ensure that they reflect in a timely way the results of studies.

TITLE V. BEST PHARMACEUTICALS FOR CHILDREN ACT OF 2007

Title V reauthorizes for five years FDA's authority to grant an additional six months of marketing exclusivity to a manufacturer of a drug in return for FDA-requested pediatric use studies and reports. Title V also includes provisions to encourage pediatric research for products that are off-patent or for products whose manufacturer declines to conduct FDA-related studies.

Title V increases to 180 days the time limit that the Secretary has for deciding whether or not to grant exclusivity. This title also

strengthens labeling requirements to ensure that labels reflect study results in a timely and consistent fashion.

TITLE VI. REAGAN-UDALL FOUNDATION

Title VI creates the Reagan-Udall Foundation for the Food and Drug Administration. The purpose of the Foundation is to establish a private-public partnership to advance FDA's Critical Path Initiative to modernize medical product development, accelerate innovation, and enhance product safety. Title VI sets forth the duties of the Foundation to include identifying unmet needs in the sciences of developing, manufacturing, and evaluating the safety and effectiveness of diagnostics, devices, biologics, and drugs. Other duties include establishing goals and priorities to meet the identified unmet needs, and awarding grants to advance the goals and priorities identified.

TITLE VII. CONFLICTS OF INTEREST

Title VII requires all individuals under consideration for appointment to serve on an advisory committee to disclose to the HHS Secretary all financial interests that would be affected by the advisory committee's actions. The Secretary may grant no more than one conflict of interest waiver per committee meeting for an individual if the individual's expertise is necessary for the work of the advisory committee. Disclosure of the waiver must be made public 15 or more days prior to the meeting of the advisory committee and must be posted on the Internet. Title VII spells out a process to allow experts with a financial conflict of interest to present information to the committee.

Title VII enhances FDA's outreach activities for identifying nonconflicted experts to participate on advisory committees and directs the Secretary to review guidance on conflict of interest waiver determinations with respect to advisory committees at least once every five years and update this guidance as necessary.

TITLE VIII. CLINICAL TRIAL DATABASES

Title VIII establishes two separate databases: one for a clinical trials registry and the other for clinical trials results. All clinical trials that are conducted to test the safety and efficacy of either drugs or devices would be subject to the database reporting requirements. The databases would apply to both privately and publicly-funded clinical trials. Title VIII requires the clinical trials registry and clinical trials results database to be made publicly available through the Internet. Title VIII provides civil monetary penalties (CMPs) for noncompliance.

TITLE IX. RISK EVALUATION AND MITIGATION STRATEGIES

Title IX strengthens FDA's postmarket drug safety authority and provides greater FDA transparency. Specifically, Title IX provides FDA with the authority to require labeling changes under appropriate circumstances and provides for an increased level of civil monetary penalties for violations of the Federal Food, Drug, and Cosmetic Act. Title IX provides FDA with a process to prereview television pharmaceutical advertisements. Specifically, this title strengthens FDA's ability to monitor and remedy false and mis-

leading television advertising and provides an administrative procedure and CMPs for violations.

Title IX provides FDA with enhanced tools to ensure postmarket drug safety through a "Risk Evaluation and Mitigation Strategy" (REMS) process. This title grants the Secretary the authority to require a REMS, if the Secretary determines it is necessary to ensure that the benefits of the drug involved outweigh the risks of the drug, for new drug and biologic license applications, for drugs and biologics that have already been approved, and for supplemental applications seeking approval of a new indication for use of the drug. Title IX requires FDA to review data on the use of drug products after they have been on the market for at least seven years. It also directs the Secretary to establish an active postmarket drug surveillance infrastructure.

BACKGROUND AND NEED FOR LEGISLATION

The mission statement of the U.S. Food and Drug Administration asserts its responsibility to protect the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our Nation's food supply, cosmetics, and products that emit radiation. FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health. FDA regulates $1 trillion worth of products a year, representing 25 cents out of every consumer dollar. FDA's budget amounts to only about $6 a year for each citizen. There are a number of programs that provide FDA with resources and authority to carry out its mission. The primary focus of H.R. 2900 is FDA's programs and resources devoted to human drugs and medical devices.

Title I. Prescription Drug User Fee Amendments of 2007

The Prescription Drug User Fee Act (PDUFA), originally enacted in 1992, provides an additional revenue source for the Food and Drug Administration to supplement appropriations from Congress. These resources are used to expedite review of drug and biologic product approval applications and subsequent drug safety monitoring. PDUFA requires pharmaceutical companies to pay application fees for each new product and supplements to existing products, annual manufacturing establishment fees, and annual product fees. PDUFA expires on September 30, 2007, prompting congressional action for its third reauthorization.

Impetus for PDUFA peaked during the late 1980s, as frustration grew among industry, consumers, and Government over the length of time between submission of a product application to FDA and the agency's final approval decision. Prior to PDUFA, FDA review of a new drug or a new biologic for sale in the United States took a median time of 29 months. Industry pressed for shorter review times in order to bring their drugs and biologics to market sooner and consumers argued for faster access to potentially life-saving products. FDA, citing a lack of sufficient appropriations from Congress, concluded that they needed extra resources to hire additional scientists to expedite the review process.

Manufacturers agreed to the establishment of user fees that would be used to supplement, not replace, direct appropriations from Congress for FDA. Under the original PDUFA, user fees could only be assessed if Congressional appropriations for FDA exceeded FY1992 levels and the new drug review budget exceeded 1992 levels. These fees were used to meet performance goals, mutually agreed upon by FDA and manufacturers. The Commissioner of Food and Drugs is required to send these goals to the Chairman of the Committee on Energy and Commerce of the U.S. House of Representatives and the Chairman of the Committee on Health, Education, Labor and Pensions of the U.S. Senate for inclusion in the Congressional Record.

The original 1992 law establishing user fees, PL 102–571, commonly referred to as PDUFA I, was reauthorized in 1997 (PDUFA II) and 2002 (PDUFA III). Each reauthorization has built upon the foundation of PDUFA I by adding components for decreased review times and increased consumer safety. PDUFA I required FDA to review and act on a progressively increasing proportion of original new drug applications (NDAs), biologic license applications (BLAs), and efficacy supplements within 12 months and resubmissions and manufacturing supplements within 6 months. FDA was also required to review and act on 90 percent of priority NDAs, BLAs, and efficacy supplements submitted in FY1997 within 6 months. PDUFA II shortened review time expectations and expanded the scope of PDUFA work by including new goals intended to improve communication between FDA and application sponsors during the drug development process. PDUFA III, for the first time, required FDA to meet with interested public and private stakeholders when considering the reauthorization of the program. PDUFA III also gave FDA the authority to use fees to support postmarketing surveillance and risk management activities for up to three years.

User fees are a substantial part of FDA's budget. The FY2006 program level for FDA's human drugs program was approximately $517.5 million, of which 42.5 percent was from user fees. The median time between an application for a new drug or biologic license has decreased from 29 months in 1987 to less than 14 months in fiscal year 2003. HHS has concluded that user fees have resulted in significant increases in patient access to new drugs and biologics. From fiscal year 1993 through October 31, 2006, FDA has approved 1,103 NDAs and 117 BLAs, including 76 new cancer drugs; 111 drugs for metabolic and endocrine disorders; 178 anti-infective drugs (including 56 for treatment of HIV or hepatitis); 115 drugs for neurologic and psychiatric disorders; and 80 drugs for cardiovascular and renal disease. Over time, the proportion of user fees for FDA's drug programs has increased relative to appropriations. This is due to limited increases in appropriations for FDA. One concern heard by the Committee from almost every witness who testified at hearings this year was the need to provide more resources for FDA, and the best source of those resources would be appropriated funds. This legislation cannot address that concern, but it is noted for the record.

Title II. Medical Device User Fee Amendments of 2007

The Medical Device User Fee and Modernization Act (MDUFMA), originally enacted in 2002, provides an additional rev-

enue source for the Food and Drug Administration to supplement appropriations from Congress. These user fees provide FDA with additional resources to review medical devices. MDUFMA amended the Federal Food, Drug, and Cosmetic Act in three significant ways: (1) it established user fees for premarket review of devices; (2) it allowed establishment inspections to be conducted by accredited persons (third parties); and (3) it instituted new regulatory requirements for reprocessed single-use devices.

FDA's authority to collect medical device user fees expires on October 1, 2007, prompting congressional action for reauthorization. Without a timely reauthorization, FDA would be forced to carry out a reduction-in-force (RIF) that could result in the loss of a number of employees who currently review medical device applications.

Unsafe medical devices can have serious consequences for consumers that are deadly or far reaching. Problems with the procedures and equipment for HIV and hepatitis C laboratory tests led to hundreds of incorrect test results in 2004. Defects in other types of medical devices, such as pacemakers, defibrillators, and coronary stents, have caused patient deaths. Consequences such as these have raised questions as to whether adequate enforcement tools, resources, and processes are in place to ensure that marketed devices are safe.

In the years preceding enactment of MDUFMA, FDA's medical device program suffered a long-term, significant loss of resources that undermined the program's capacity and performance. Many reviews of premarket approval applications were delayed because necessary expertise was stretched thin or unavailable, and many guidance documents were out-of-date. In response, leaders of the device industry, FDA, and Congress initiated discussions about linking new user fees to increased appropriations to augment the resources available for device review. MDUFMA was influenced by those discussions.

FDA collects user fees that fund the device review process under the authority of MDUFMA. Over the period of FY2003 to FY2008, MDUFMA funding has increased at a much faster rate (220.1 percent) than FDA's program-level device review budget (31.3 percent). MDUFMA fees comprised less than 7 percent of FDA's program-level device review budget in FY2003, and estimates are that they will comprise more than 16 percent in FY2008.

A number of technical corrections were made to MDUFMA in 2004 when Congress enacted the Medical Devices Technical Corrections Act (MDTCA). MDTCA clarified some potentially confusing language in MDUFMA; modified important features of the provisions for third-party inspections; expanded the provision for electronic labeling, delayed the effective date of section 502(u) of the Food, Drug and Cosmetic Act (FDCA), which required a device to "prominently and conspicuously" bear the name of its manufacturer; and required FDA to prepare and submit to Congress a report on barriers to the availability of devices intended for children.

FDA and the medical device industry supported MDUFMA. It did not take long, however, before they realized that progress would be limited by financial shortfalls and uncertainties. MDUFMA outlined both the amount Congress was expected to appropriate to the program and the amount expected to be collected in user fees for each fiscal year. In practice, however, the user fee

framework under MDUFMA created uncertainty for industry and FDA regarding the annual increase in fees and the amount of funds that would be collected by the Agency in any given year. The amount of fees collected in a given year was unpredictable because of fluctuations in the number of applications FDA received and the number of applications received for which fees may be reduced because of a small business exemption. MDUFMA granted FDA the power to apply a "compensating judgment" that could lead to escalating fee rates if fee revenue expectations were not met. This led to substantial increases in fees and uncertainty for industry.

By May 2005, uncertainty as to whether corrective legislation would be enacted before the October 1, 2005 appropriations "trigger" date required FDA to impose a hiring freeze in its Center for Devices and Radiological Health. FDA was also faced with the difficult task of developing a workable approach to implement section 502(u) of the FDCA.

In response to the growing problems with the user fee program, Congress enacted the Medical Device User Fee Stabilization Act of 2005 (the Stabilization Act). This Act repealed the appropriations trigger for FY2003 and FY2004 and allowed for tolerances of up to 1 percent of the appropriations trigger for FYs2005–2007; provided for predictable application fees by establishing fixed annual fees for FY2006 and FY2007, although at a lower rate of increase than under the original legislation; and expanded the definition of "small business" for FY2006 and FY2007. The new law also limited section 502(u) to reprocessed single-use devices and eliminated the granting by FDA of device-specific waivers.

Title III. Pediatric Medical Device Safety and Improvement Act

Pediatric medical devices are used to treat or diagnose diseases and conditions in patients from birth through age 21. Some products are designed specifically for children, while others are borrowed from adult applications or produced for more general use.

Children have specific medical needs that must be considered when medical and surgical devices are prescribed. Devices that have not been studied for use in children may not accommodate the unique needs of children, such as allowing for expandable growth, and accommodating their active lifestyles and differing metabolism.

FDA addressed premarket review of medical devices intended for pediatric patients by issuing a guidance in May 2004 entitled, Premarket Assessment of Pediatric Medical Devices. The guidance was published pursuant to the Medical Device User Fee and Modernization Act, which contained several provisions intended to promote the development of safe and effective pediatric devices. In this guidance, FDA defined the age ranges for pediatric subpopulations, identified the types of information needed to provide reasonable assurance of the safety and effectiveness of medical devices intended for use in the pediatric population, and described the protections that sponsors should consider for pediatric subjects involved in device clinical trials.

MDUFMA also called for the Institute of Medicine (IOM) to evaluate FDA's postmarket surveillance of pediatric medical devices. The subsequent report found that FDA lacked effective procedures to monitor the status of safety studies of medical devices and recommended that Congress ensure that the agency establish a re-

liable system to track these postmarket studies. Additionally, the report found that it was difficult to reliably identify postmarket studies that considered pediatric issues or that more generally focused on children. The report also recommended that FDA, NIH, Agency for Healthcare Research and Quality, and other research funding agencies and interested parties set priorities for research on unanswered questions about the safe use of devices for children.

The Medical Devices Technical Corrections Act of 2004, required the Secretary of HHS to submit a "report on the barriers to the availability of devices intended for the treatment or diagnosis of diseases and conditions that affect children." This report was completed in October 2004. To prepare the report, FDA sought comment from interested parties through participation in a stakeholder meeting and by publishing a notice in the Federal Register requesting comment. HHS concluded that it was premature to recommend any substantive policy changes, including administrative and legislative changes.

Titles IV–V. Pediatric Research Equity Act of 2007; Best Pharmaceuticals for Children Act of 2007

Approximately 75 percent of drugs and a large majority of devices used in pediatric medicine have not been appropriately tested for use in children. Clinicians, however, often prescribe them for children believing that the safety and effectiveness demonstrated with adults will apply to younger patients. Unfortunately, this off-label prescribing can result in children receiving ineffective drugs or too much or too little of a potentially useful drug. Some side effects are unique to children or children of specific ages, including effects on growth and development. Studies show that drugs vary in bioavailability in children, which depends on the maturation and development of organs and other factors.

The market for any individual drug's pediatric indications is generally small, providing an economic disincentive for manufacturers to commit resources to pediatric testing. The result is that few marketed drugs have been tested for safety and effectiveness in children. In some tragic cases, children have died or suffered serious injury as a result of either taking drugs that are shown safe for use in adults or from a medical device that worked properly in adults, but had different results when used in children. A March 2007 study, "Off-label Drug Use in Hospitalized Children," published in the Archives of Pediatric Adolescent Medicine, found that 78.7 percent of pediatric patients discharged from the hospital during the time period of the study used at least one drug off-label.

Prior to the enactment of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), most therapies commonly used by children failed to provide instructions for pediatric use. Historically, approximately 80 percent of medication labels in the Physician's Reference Directory did not have pediatric use information. At least 62 percent of drugs on the market were unstudied and labeled for pediatric use. Only 38 percent of new drugs potentially useful in pediatrics were labeled for children when initially approved.

Pediatric exclusivity was intended to provide a substantial incentive for sponsors to conduct some pediatric studies. The pediatric rule was intended to increase the number of drug and biological

products that have adequate labeling by granting FDA authority to require pediatric studies. Because of the voluntary nature of the incentive provided by the Food and Drug Administration Modernization Act of 1997 (FDAMA) and BPCA, the possibility arose that many drugs might never have been studied for pediatric uses.

On December 2, 1998, FDA published in the Federal Register a final regulation known as the 'Pediatric Rule,' asserting the authority to require all manufacturers to submit pediatric testing data upon submittal of all new drug and biologic applications. On October 17, 2002, a Federal court held that FDA lacked the statutory authority to promulgate the Pediatric Rule, and declared the rule invalid.

In response to the court decision, Congress enacted PREA, which essentially codified the Pediatric Rule by adding a new section 505B to the FFDCA. With PREA, a manufacturer submitting an application to market a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration must at the same time submit a pediatric assessment. If the disease course and drug effects are sufficiently similar for adults and children, the HHS Secretary may allow extrapolation from adult study data as evidence of pediatric effectiveness, usually supplemented with other data from children, such as pharmacokinetic studies. PREA specifies situations in which the HHS Secretary may defer or waive the pediatric assessment requirement.

For products already on the market, PREA grants the HHS Secretary the authority to require the manufacturer of an approved drug or licensed biologic to submit a pediatric assessment in situations in which the absence of pediatric use information on the label could pose significant risks. Before requiring the assessment, the Secretary must have issued a written request under FFDCA Section 505A or Public Health Service Act (PHSA) Section 409I. Further, the manufacturer must not have agreed to conduct the assessment, and the Secretary must have stated that the NIH funding programs either have or do not have sufficient funds to conduct that study. If the manufacturer does not comply with the Secretary's notice of a required study, the Secretary may consider the product misbranded. Because Congress wanted to protect adult access to a product under these circumstances, the law sets limits on FDA's enforcement options, precluding, for example, the withdrawal of approval or license to market.

In January of 2002, Congress passed the Best Pharmaceuticals for Children Act as part of its second major attempt to increase the number of clinical tests performed on pediatric populations. Congress's earlier effort to promote pediatric clinical testing was the pediatric exclusivity provision of FDAMA. With FDAMA, Congress provided an incentive: in exchange for a manufacturer's completion of pediatric studies, performed voluntarily or in response to an FDA written request, FDA would extend its market exclusivity for that product for six months. Enacted in 2002, BPCA reauthorized this program for five years.

BPCA renewed FDA's authority to give an additional six month period of marketing exclusivity to a manufacturer in return for FDA-requested pediatric use studies and reports. Since pediatric exclusivity, as originally defined in FDAMA, did not apply to products no longer covered by patent (off-patent) or other marketing ex-

clusivity agreements, and since patent holding manufacturers could decline to conduct FDA-requested studies, BPCA added provisions to encourage pediatric research in those products. For off-patent products, BPCA added a new section, 409I, to the Public Health Service Act, which established an off-patent NIH research fund for these studies and authorized appropriations of $200 million for FY2002 and such sums as are necessary for each of the five years until the provisions sunset on October 1, 2007. For on-patent drugs whose manufacturers declined FDA's written requests for studies, BPCA amended the Federal Food, Drug, and Cosmetic Act Section 505A to allow their referral by FDA to the NIH Foundation for pediatric studies.

BPCA also granted pediatric supplemental applications priority status to address the concern that pediatric exclusivity did not lead to quick changes in drug labels. Further, the legislation provided for a dispute resolution mechanism for labeling changes that have not been resolved within 180 days of supplement submission. At the end of this process, should the manufacturer not agree to comply with the Secretary's proposed label, the Secretary may 'deem' the drug misbranded.

Pediatric exclusivity has resulted in more than 132 completed studies leading to over 114 label changes incorporating new pediatric information. In a March 2007 report to Congress entitled Pediatric Drug Research: Studies Conducted Under Best Pharmaceuticals for Children Act, the U.S. Government Accountability Office (GAO) noted that these labeling changes were often made as a result of findings by the pediatric drug studies that children may have been exposed to ineffective drugs, ineffective dosing, overdosing, or previously unknown side effects. These studies underscore the danger of assuming that because a drug that is safe and effective in adults, it is also safe and effective in children.

Titles VI–IX. Reagan-Udall Foundation; Conflicts of Interest; Clinical Trials Databases; Risk Evaluation and Mitigation Strategies

Following several high-profile drug safety cases in 2004, the GAO wrote a report in March 2006 entitled, Drug Safety: Improvement Needed in FDA's Postmarket Decision-Making and Oversight Process. In its report, the GAO found that FDA lacked clear and effective processes for making decisions about, and providing management oversight of, postmarket drugs safety issues. Specific problems cited included: a lack of criteria for determining what safety action to take and when to take them; insufficient communication between the Office of New Drugs (OND) and the Office of Drug Safety (ODS); FDA's access to data being constrained by its limited authority to require drug sponsors to conduct postmarket studies; and FDA's limited resources for acquiring data from other external sources.

FDA then commissioned the Institute of Medicine to write a report on drug safety. In its report, The Future of Drug Safety: Promoting and Protecting the Health of the Public, IOM raised several concerns: FDA and the pharmaceutical industry do not consistently demonstrate accountability and transparency to the public about safety concerns in a timely and effective fashion; the drug safety system is impaired by serious resource constraints that weaken the

quality and quantity of the science; and an organizational structure in the Center for Drug Evaluation and Research (CDER) is not functioning properly and being hindered by unclear, insufficient regulatory authority.

Four titles in this bill address the concerns raised by the GAO and IOM reports: Reagan-Udall Foundation, Conflicts of Interest for FDA Advisory Committees, Clinical Trials Registry Database and Clinical Trials Results Database, and Risk Evaluation and Mitigation Strategies (REMS).

Title VI, the Regan-Udall Foundation, addresses the concern that, over the last decade, fewer new medical products have been submitted to the FDA for approval because the use of outmoded testing methods is resulting in a rising product failure rate during development. Newer technologies need new methods for their assessment. Allowing FDA to collaborate with other researchers will contribute greatly to filling this void.

Title VII addresses concerns that advisory panels play an important role in FDA's work, and therefore, the advice provided by these panels should not be influenced by conflicts of interest. FDA relies heavily on the recommendations of its 30 advisory committees in its assessment of product safety and benefit. There has been concern that members of these committees may not be operating in the most judicious manner due to industry funding or other financial interests. It is important that more safeguards are put into place to ensure that advisory committee members are serving with integrity and with the best interest of the consumer in mind.

Title VIII establishes a comprehensive, mandatory clinical trials registry database and clinical trials results database. This addresses concerns raised by the IOM's report on drug safety in regard to the need for FDA to increase the availability of information to the public and to researchers for recruitment purposes and to communicate the risks and benefits of drugs. Currently, the NIH database, ClinicalTrials.gov, hosts information only on trials for serious or life-threatening conditions. The Committee believes that information about trial results is important to providers and patients. Presently, negative results may or may not be released by sponsors. A uniform, centralized database and registry will help patients, providers, and researchers learn new information and make more informed healthcare decisions.

Title IX is the centerpiece of this bill's attempt to enhance postmarket drug safety. A central aspect of this program is to authorize FDA to require a risk evaluation and mitigation strategy (REMS) in all appropriate cases. The IOM report highlights the need to extend drug safety consideration from premarket through postmarket approval. A number of other reports suggest that cultural issues within FDA and gaps in the agency's authorities hamper the ability to take swift and effective action when problems arise. The REMS program will be enhanced by the establishment of a robust active surveillance program designed to see how drugs work in real world postmarket circumstances, which are often quite different than what is learned about a drug in the carefully controlled clinical trial setting.

HEARINGS

There were four oversight hearings and one legislative hearing held by the Committee's Subcommittee on Health in connection to the bill reported by the Committee.

The Subcommittee on Health held a hearing on "Reauthorization of the Prescription Drug User Fee Act" on Tuesday, April 17, 2007. The Subcommittee received testimony from the following: Theresa M. Mullin, Ph.D., Assistant Commissioner for Planning, Food and Drug Administration (FDA); Alan Goldhammer, Ph.D., Deputy Vice President for Regulatory Affairs, Pharmaceutical Research and Manufacturers of America (PhRMA); Mr. James Thew, Patient Advocate, Amyotrophic Lateral Sclerosis (ALS) Association; Ms. Kay Holcombe, Senior Policy Advisor, Genzyme Corporation; Mr. William K. Vaughan, Senior Policy Advocate, Consumers Union; and Mr. William Hubbard, Senior Advisor, Coalition for a Stronger FDA.

The Subcommittee on Health held a hearing on "Assessing the Safety of our Nation's Drug Supply" on Wednesday, May 9, 2007. The Subcommittee received testimony from the following: Steven K. Galson, M.D., M.P.H., Director, Center for Drug Evaluation and Research, Food and Drug Administration; Marcia Crosse, Ph.D., Director, Health Care Issues, U.S. Government Accountability Office; Susan S. Ellenberg, Ph.D., Associate Dean for Clinical Research, University of Pennsylvania School of Medicine; Sharon Levine, M.D., Associate Executive Director, The Permanente Medical Group; Caroline Loew, Ph.D., Senior Vice President, Science and Regulatory Affairs, PhRMA; John H. Powers, III, M.D., F.A.C.P., F.I.D.S.A. (formerly of FDA); Ellen V. Sigal, Ph.D., Friends of Cancer Research; Ms. Lisa Van Syckel; Mr. R. John Theriault, Chief Security Officer and Vice President, Global Security, Pfizer, Inc.; and Ms. Diane Thompson, Vice President, Public Policy and Communications, Elizabeth Glaser Pediatric AIDS Foundation (on behalf of the Alliance for Drug Safety and Access).

The Subcommittee on Health held a hearing on "Reauthorization of the Medical Device User Fee and Modernization Act" on Wednesday, May 16, 2007. The Subcommittee received testimony from the following: Jeffrey Shuren, M.D., J.D., Assistant Commissioner for Policy, FDA; Paul LaViolette, M.B.A., Chief Operating Officer, Boston Scientific Corporation; Diana Zuckerman, Ph.D., President, National Research Center for Women and Families; Mr. Kelvyn Cullimore, Jr., President and CEO, Dynatronics Corporation, and Secretary, Medical Device Manufacturers Association; Mr. Steven A. Grossman, Executive Director, The FDA Alliance; and Ms. Diane E. Dorman, Vice President for Public Policy, National Organization for Rare Disorders (NORD).

The Subcommittee on Health held a hearing on "Programs Affecting Safety and Innovation in Pediatric Therapies" on Tuesday, May 22, 2007. The Subcommittee received testimony from the following: RADM Sandra L. Kweder, M.D., Deputy Director, Office of New Drugs, Center for Drug Evaluation and Research, FDA; Donald Mattison, M.D., Chief, Obstetric and Pediatric Pharmacology Branch, National Institute of Child Health and Human Development, NIH; Ms. Lori Reilly, Vice President for Policy and Research, PhRMA; Marcia Crosse, Ph.D., Director, Health Care Issues, U.S.

Government Accountability Office; Richard L. Gorman, M.D., F.A.A.P., Chair, AAP Section on Clinical Pharmacology and Therapeutics, American Academy of Pediatrics (AAP); Peter Lurie, M.D., M.P.H., Deputy Director, Public Citizen's Health Research Group; Mr. Donald P. Lombardi, President and CEO, Institute for Pediatric Innovation; Ed Rozynski, Vice President, Global Government Affairs, Stryker Corporation; and Ms. Susan Belfiore, testifying on behalf of the Elizabeth Glaser Pediatric AIDS Foundation.

The Subcommittee on Health held a legislative hearing on "Discussion Drafts Concerning Prescription Drug User Fee Act Reauthorization, Medical Device User Fee and Modernization Act Reauthorization, Drug Safety, and Certain Pediatric Pharmaceutical and Device Legislation" on Tuesday, June 12, 2007. The Subcommittee received testimony from the following: Randall L. Lutter, Ph.D., Associate Commissioner for Policy and Planning, FDA; Richard L. Gorman, M.D., F.A.A.P., Chair, AAP Section on Clinical Pharmacology and Therapeutics, American Academy of Pediatrics; Diana Zuckerman, Ph.D. President, National Research Center for Women and Families; Caroline Loew, Ph.D., Senior Vice President, Science and Regulatory Affairs, PhRMA; Mr. Steve Walker, Co-Founder and Chief Advisor, Abigail Alliance for Better Access to Developmental Drugs; Mr. James Guest, President and CEO, Consumers Union; and Mr. Steven J. Ubl, President and CEO, Advanced Medical Technology Association.

SUBCOMMITTEE CONSIDERATION

Prior to the introduction of H.R. 2900, its text was considered in the Committee as nine separate Committee Prints, each of which became one of the titles of the bill.

On Tuesday, June 19, 2007, the Subcommittee on Health met in open markup session and took the following actions on the nine Committee Prints:

The Committee Print on the Prescription Drug User Fee Amendments of 2007 (PDUFA) was favorably forwarded to the full Committee, amended, by a voice vote.

The Committee Print on the Medical Device User Fee Amendments of 2007 (MDUFA) was favorably forwarded to the full Committee, amended, by a voice vote.

The Committee Print on the Pediatric Medical Device Safety and Improvement Act of 2007 was favorably forwarded to the full Committee, without amendment, by a voice vote.

The Committee Print on the Pediatric Research Equity Act of 2007 was favorably forwarded to the full Committee, amended, by a voice vote.

The Committee Print on the Best Pharmaceuticals for Children Act of 2007 was favorably forwarded to the full Committee, amended, by a voice vote.

The Committee Print to amend the Federal Food, Drug, and Cosmetic Act to provide for the establishment of the Reagan-Udall Institute for Applied Biomedical Research, and for other purposes, was favorably forwarded to the full Committee, amended, by a voice vote.

The Committee Print to amend the Federal Food, Drug, and Cosmetic Act with respect to conflicts of interest, and for other

purposes, was favorably forwarded to the full Committee, without amendment, by a voice vote.

The Committee Print to amend the Public Health Service Act to provide for the establishment of a clinical trial registry database and a clinical trial results database, and for other purposes, was favorably forwarded to the full Committee, amended, by a voice vote.

The Committee Print to amend the Federal Food, Drug, and Cosmetic Act to improve drug safety, and for other purposes, was favorably forwarded to the full Committee, amended, by a voice vote.

COMMITTEE CONSIDERATION

On Thursday, June 21, 2007, the full Committee met in open markup session and considered the nine Committee Prints, each of which was ordered favorably reported to the House, amended, by a voice vote, except that the Committee Print to amend the Federal Food, Drug, and Cosmetic Act with respect to conflicts of interest, and for other purposes, was ordered favorably reported to the House, without amendment, by a voice vote.

By unanimous consent, the full Committee then agreed that the nine Committee Prints, as ordered reported, be combined and introduced as a single bill and reported favorably to the House without further consideration by the Committee. Pursuant to that agreement, the Committee ordered the single bill favorably reported, by a recorded vote of 43–0.

COMMITTEE VOTES

Clause 3(b) of rule XIII of the Rules of the House of Representatives requires the Committee to list the record votes on the motion to report legislation and amendments thereto. Mr. Pallone moved that, pursuant to the agreement to introduce a single bill consisting of the nine approved Committee Prints, a recorded vote be held to report the single bill favorably to the House. The motion to report the single bill favorably to the House was agreed to by a recorded vote of 43 yeas and 0 nays. The following are the recorded votes taken on the motion and on amendments, including the names of those Members voting for and against.

COMMITTEE ON ENERGY AND COMMERCE -- 110TH CONGRESS
ROLL CALL VOTE # 15

BILL: H.R. _____, Committee Print to amend the Federal Food, Drug, and Cosmetic Act to provide for the establishment of the Reagan-Udall Foundation for the Food and Drug Administration, and for other purposes.

AMENDMENT: An amendment to the Pallone amendment by Mr. Doyle, No. 1b, on page 5, line 1, strike "$5,000,000" and insert "$25,000,000".

DISPOSITION: **NOT AGREED TO**, by a roll call vote of 14 yeas to 24 nays.

REPRESENTATIVE	YEAS	NAYS	PRESENT	REPRESENTATIVE	YEAS	NAYS	PRESENT
Mr. Dingell		X		Mr. Barton		X	
Mr. Waxman	X			Mr. Hall		X	
Mr. Markey				Mr. Hastert			
Mr. Boucher				Mr. Upton			
Mr. Towns		X		Mr. Stearns			
Mr. Pallone		X		Mr. Gillmor[1]			
Mr. Gordon				Mr. Deal		X	
Mr. Rush		X		Mr. Whitfield		X	
Ms. Eshoo				Mrs. Cubin			
Mr. Stupak	X			Mr. Shimkus		X	
Mr. Engel		X		Mrs. Wilson	X		
Mr. Wynn	X			Mr. Shadegg			
Mr. Green		X		Mr. Pickering			
Ms. DeGette		X		Mr. Fossella			
Mrs. Capps	X			Mr. Buyer			
Mr. Doyle	X			Mr. Radanovich			
Ms. Harman	X			Mr. Pitts		X	
Mr. Allen				Ms. Bono		X	
Ms. Schakowsky		X		Mr. Walden		X	
Ms. Solis		X		Mr. Terry	X		
Mr. Gonzalez		X		Mr. Ferguson			
Mr. Inslee	X			Mr. Rogers			
Ms. Baldwin	X			Mrs. Myrick		X	
Mr. Ross		X		Mr. Murphy	X		
Ms. Hooley	X			Mr. Burgess		X	
Mr. Weiner				Ms. Blackburn		X	
Mr. Matheson		X					
Mr. Butterfield	X						
Mr. Melancon							
Mr. Barrow		X					
Mr. Hill	X						

06/21/2007

[1] *Pursuant to H. Res. 496, agreed to by the House on June 19, 2007, Mr. Gillmor of Ohio was elected to the Committee on Energy and Commerce to rank after Mr. Stearns of Florida, during a leave of absence by Mr. Sullivan of Oklahoma. Mr. Deal of Georgia also asked unanimous consent on June 19, 2007, during a markup of the Subcommittee on Health, to permit Mr. Gillmor to serve on the Subcommittee on Health during his service on the full Committee, during the absence of Mr. Sullivan. There was no objection to the request by the Subcommittee on Health. Subsequently, the House agreed to H. Res. 520 on June 27, 2007, electing Mr. Sullivan to rank after Mrs. Myrick on the Committee on Energy and Commerce.*

COMMITTEE ON ENERGY AND COMMERCE -- 110TH CONGRESS
ROLL CALL VOTE # 16

BILL: Nine Committee Prints relating to Food and Drug legislation, as adopted by the Committee.

MOTION: A motion by Mr. Pallone that, pursuant to the unanimous consent agreement by the Committee regarding introducing a single bill consisting of the approved language of the nine Committee Prints on FDA legislation, the single bill be favorably reported to the House.

DISPOSITION: AGREED TO, by a roll call vote of 43 yeas to 0 nays.

REPRESENTATIVE	YEAS	NAYS	PRESENT	REPRESENTATIVE	YEAS	NAYS	PRESENT
Mr. Dingell	X			Mr. Barton	X		
Mr. Waxman	X			Mr. Hall	X		
Mr. Markey	X			Mr. Hastert			
Mr. Boucher				Mr. Upton			
Mr. Towns	X			Mr. Stearns			
Mr. Pallone	X			Mr. Gillmor			
Mr. Gordon				Mr. Deal	X		
Mr. Rush	X			Mr. Whitfield	X		
Ms. Eshoo	X			Mrs. Cubin			
Mr. Stupak	X			Mr. Shimkus	X		
Mr. Engel	X			Mrs. Wilson	X		
Mr. Wynn	X			Mr. Shadegg	X		
Mr. Green	X			Mr. Pickering			
Ms. DeGette	X			Mr. Fossella	X		
Mrs. Capps	X			Mr. Buyer	X		
Mr. Doyle	X			Mr. Radanovich			
Ms. Harman	X			Mr. Pitts	X		
Mr. Allen				Ms. Bono	X		
Ms. Schakowsky	X			Mr. Walden	X		
Ms. Solis	X			Mr. Terry	X		
Mr. Gonzalez	X			Mr. Ferguson			
Mr. Inslee	X			Mr. Rogers			
Ms. Baldwin	X			Mrs. Myrick	X		
Mr. Ross	X			Mr. Murphy	X		
Ms. Hooley	X			Mr. Burgess	X		
Mr. Weiner				Ms. Blackburn	X		
Mr. Matheson	X						
Mr. Butterfield	X						
Mr. Melancon							
Mr. Barrow	X						
Mr. Hill	X						

06/21/2007

COMMITTEE OVERSIGHT FINDINGS

Pursuant to clause 3(c)(1) of rule XIII of the Rules of the House of Representatives, the Subcommittee on Health has held legislative and oversight hearings on this legislation and made findings that are reflected in this report.

STATEMENT OF GENERAL PERFORMANCE GOALS AND OBJECTIVES

The objectives of H.R. 2900 are to reauthorize prescription drug and medical device user fee programs; ensure that drugs and devices used in children are properly studied and labeled for pediatric use; and improve prescription drug and medical device safety and oversight.

NEW BUDGET AUTHORITY, ENTITLEMENT AUTHORITY, AND TAX EXPENDITURES

Regarding compliance with clause 3(c)(2) of rule XIII of the Rules of the House of Representatives, the Committee finds that H.R. 2900 would result in no new or increased budget authority, entitlement authority, or tax expenditures. As described in the cost estimate included below (from the Director of the Congressional Budget Office), new receipts would result under section 901(d)(4) of the bill, which amends section 303 of the Federal Food, Drug, and Cosmetic Act to add a subsection (g) that provides for civil money penalties.

EARMARKS AND TAX AND TARIFF BENEFITS

In compliance with clause 9 of rule XXI of the Rules of the House of Representatives, H.R. 2900 does not contain any congressional earmarks, limited tax benefits, or limited tariff benefits as defined in clause 9(d), 9(e), or 9(f) of rule XXI.

COMMITTEE COST ESTIMATE

The Committee adopts as its own the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

CONGRESSIONAL BUDGET OFFICE ESTIMATE

Pursuant to clause 3(c)(3) of rule XIII of the Rules of the House of Representatives, the following is the cost estimate provided by the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974:

H.R. 2900—Food and Drug Administration Amendments of 2007

Summary: H.R. 2900 would authorize the collection and spending of user fees by the Food and Drug Administration (FDA) for certain activities to expedite the marketing approval of prescription drugs and medical devices and to regulate prescription drugs after they enter the market. Such fees would be collected and made available for obligation only to the extent and in the amounts provided in advance in appropriation acts.

The bill also would establish a surveillance system to monitor and assess the safety profile of drugs on the market, enhance

FDA's authority to regulate marketed drugs, expand federal databases that track information on certain clinical trials, and reauthorize and modify programs that evaluate the use of drugs and devices by children. The legislation would authorize funds to extend FDA's grant program for orphan products, conduct post-marketing surveillance of medical devices, establish programs to accelerate innovation and improve the evaluation of medical products, and promote the security of drugs distributed in the United States.

On balance, CBO estimates that implementing H.R. 2900 would have net discretionary costs of $728 million over the 2008–2012 period. Enacting the bill would increase direct spending by $7 million over the 2009–2012 period and by $200 million over the 2009–2017 period. Finally, we estimate that enacting H.R. 2900 would decrease net federal revenues by $1 million over the next five years and by $41 million over the 10 years through 2017.

H.R. 2900 contains both intergovernmental and private-sector mandates as defined in the Unfunded Mandates Reform Act (UMRA). The bill would preempt any state or local law that requires manufacturers of medical devices or drugs to register clinical trails and related information in a database, but the net costs of that mandate would be minimal and far below the threshold established in UMRA ($66 million in 2007, adjusted annually for inflation). The most costly of the bill's private-sector mandates would be the requirement that manufacturers of prescription drugs and medical devices pay fees to the FDA. The direct cost of the fees would exceed the annual threshold specified in UMRA ($131 million in 2007, adjusted annually for inflation).

Estimated Cost to the Federal Government: H.R. 2900 would affect discretionary and direct spending, as well as revenues. (See Tables 1 and 2 at the end of this estimate). The costs of this legislation fall primarily within budget functions 550 (health) and 570 (Medicare). It would also affect budget functions 370 (commerce and housing credit), 700 (veterans benefits and services), and 750 (administration of justice).

Spending subject to appropriation

Assuming appropriation action consistent with the bill, CBO estimates that implementing H.R. 2900 would reduce net discretionary outlays by $100 million in 2008, primarily because the spending of fees lags somewhat behind their collection. CBO estimates that gross spending in subsequent years would exceed the amounts collected from user fees (because some of that spending under the bill would not be offset by fees), and that the net cost of implementing the bill would amount to $728 million over the 2008–2012 period, assuming the appropriation of the necessary amounts (see Table 1).

Because a significant portion of the cost of FDA activities would be offset by user fees, the largest component of the net discretionary cost of implementing H.R. 2900 would be an estimated $432 million in spending over the 2008–2012 period mostly for pediatric research conducted by the National Institutes of Health. It is unclear how a provision in the bill (in section 103) would be implemented. The provision would require FDA to reduce annual assessments for user fees dedicated to drug safety activities based, in part, on certain levels of funds appropriated for the "process of human drug review." Given that uncertainty, our estimate reflects

the full (unadjusted) collections of user fees authorized under the bill plus any funding provided by additional authorizations of appropriations.

Direct spending

H.R. 2900 also would extend the authority for FDA to administer an incentive program that grants market exclusivity to manufacturers that voluntarily conduct studies on the use of drugs in certain pediatric populations, the so-called "pediatric exclusivity program." The bill would require that affected periods of existing market exclusivity be extended by an additional six months if the manufacturer meets specified requirements. (During such period of pediatric exclusivity, FDA could not permit another manufacturer to market a version of the drug.)

Extending market exclusivity for certain prescription drugs by six months would delay the entry of lower-priced generic versions of those drugs, which would affect both direct spending and federal revenues. Because delaying the availability of lower-priced generic drugs would increase spending on pharmaceutical benefits by federal health programs, CBO estimates that direct spending for Medicare, Medicaid, the Federal Employees Health Benefits (FEHB) program, and the TRICARE for Life program would increase by an estimated $7 million over the 2009–2012 period and $200 million over the 2009–2017 period (see Table 2). (CBO estimates that the market exclusivity provisions would increase discretionary spending by the FEHB program, Department of Veterans Affairs, Department of Defense, and other federal health benefits programs by about $2 million over the 2009–2012 period. Those effects are included under "Provisions Affecting Pediatric Populations" in Table 1.)

Revenues

H.R. 2900 would affect revenues in two ways. First, it would make certain violations of new requirements under the bill subject to civil money penalties; collections of such penalties are classified as federal revenues. Second, higher spending for prescription drugs would increase the cost of premiums for private health insurance. Higher premiums, in turn, would result in more of an employee's compensation being received in the form of nontaxable employer-paid premiums, and less in the form of taxable wages. As a result of this shift, federal income and payroll tax revenues would decline. CBO estimates that the proposal would reduce net federal revenues by $1 million over the 2009–2012 period and $41 million over the 2009–2017 period (see Table 2). Social Security payroll taxes, which are off-budget, would account for $13 million of that total.

Estimated impact on State, Local, and tribal governments: H.R. 2900 would preempt any state or local law that requires manufacturers of medical devices or drugs to register clinical trials and related information in a database. That preemption would be an intergovernmental mandate as defined in the Unfunded Mandates Reform Act because it would limit the application of state and local law. While a number of states have considered legislation in recent years to establish such requirements, only a few have enacted them. In some cases, states have established fees that are tied to the registration requirements. While those states would lose a

small amount of fee revenues as a result of the preemption, costs of state regulatory responsibilities also would decline. Consequently, CBO estimates that the net costs to comply with the mandate would be minimal and far below the threshold established in UMRA ($66 million in 2007, as adjusted for inflation).

Spending by states for Medicaid would increase by an additional $35 million over the 2009–2017 period because of the provision in the bill that would delay entrance into the market of some generic drugs. Because states have flexibility in that program to adjust their financial and programmatic responsibilities, such additional spending would not result from an intergovernmental mandate.

Estimated impact on the private sector: The bill would place a number of requirements on the manufacturers of prescription drugs and medical devices that would be private-sector mandates as defined in UMRA. The most costly of those mandates would be the requirement that those entities pay fees to the FDA. CBO estimates that the direct cost of those fees alone would exceed the annual threshold specified in UMRA ($131 million in 2007, adjusted annually for inflation) in each of the five years that the mandates would be effective.

In addition to the fees on manufacturers of prescription drugs and medical devices under titles I and II, the bill contains other private-sector mandates that would impose additional but smaller costs. Title IV would renew FDA's authority to require that manufacturers undertake certain studies of the safety and efficacy of their drugs in pediatric populations. Title V would renew the Secretary's ability to award brand-name drug manufacturers six months of market exclusivity for the completion of FDA-requested pediatric studies. (The exclusivity period would effectively be a mandate on generic drug manufacturers because they would not be allowed to enter the market during that period.) Title VIII would require that manufacturers submit information about clinical trials to FDA. Title IX would enhance FDA's authority to regulate drugs by requiring that drug manufacturers submit a risk evaluation and mitigation strategy if the Secretary determines that such a strategy is necessary to protect the public's health.

Previous CBO estimate: On April 27, 2007, CBO transmitted a cost estimate for S. 1082, the Prescription Drug User Fee Amendments of 2007, as reported by the Senate Committee on Health, Education, Labor, and Pensions. Many of the provisions contained in H.R. 2900 as ordered reported by the House Committee on Energy and Commerce are contained in S. 1082. The differences between the two bills are reflected in CBO's two estimates.

H.R. 2900 differs from S. 1082 in a number of ways. For example, H.R. 2900 would provide six months of exclusivity to all drugs granted pediatric exclusivity under the program; S. 1082 would limit the pediatric exclusivity period to three months for certain "blockbuster" drugs. H.R. 2900 would also allow FDA to require that firms submit television advertisements to FDA for review prior to distribution and to make certain violations related to direct-to-consumer advertising subject to civil monetary penalties. S. 1082 does not contain a similar provision.

In addition, the bills would authorize different levels of additional user fee collections for activities related to drug safety while specifying different adjustment mechanisms for assessing such fees

in a given year. H.R. 2900 would authorize $25 million a year through 2012 to establish a surveillance system for marketed drugs compared with annual authorizations of $30 million under S. 1082.

H.R. 2900 also would authorize $25 million annually through 2012 to carry out activities related to risk evaluation and management strategies and for initiatives by several federal agencies to improve the security of drugs distributed in the United States. The bill would authorize $30 million annually over the 2008–2012 period to extend FDA's grant program for orphan products and additional funding for other activities.

In total, CBO's estimate of net discretionary spending for H.R. 2900 is $181 million higher than for S. 1082 over the 2008–2012 period. Estimates of direct spending and revenues are also different for the two bills. Over the 2009–2017 period, CBO estimates that direct spending under H.R. 2900 would be $50 million higher and total net revenue losses would be $9 million higher than for S. 1082 as reported by the Senate Committee on Health, Education, Labor, and Pensions.

Estimate prepared by: Federal Costs: Julia Christensen and Sarah Evans. Impact on State, Local, and Tribal Governments: Lisa Ramirez-Branum. Impact on the Private Sector: Anna Cook and Stuart Hagen.

Estimate approved by: Peter H. Fontaine, Deputy Assistant Director for Budget Analysis.

TABLE 1. ESTIMATED IMPACT OF H.R. 2900 ON DISCRETIONARY SPENDING

	By fiscal year, in millions of dollars—				
	2008	2009	2010	2011	2012
CHANGES IN SPENDING SUBJECT TO APPROPRIATION					
Collections from User Fees:					
Prescription Drug Fees	−463	−541	−626	−717	−886
Advertising Fees	−13	−8	−10	−10	−11
Medical Device Fees	−48	−53	−57	−62	−67
Total, Estimated Authorization Level	−524	−602	−693	−789	−964
Total, Estimated Outlays	−524	−602	−693	−789	−964
Spending of User Fees:					
Prescription Drug Fees	463	541	626	717	886
Advertising Fees	13	8	10	10	11
Medical Device Fees	48	53	57	62	67
Total, Estimated Authorization Level	524	602	693	789	964
Total, Estimated Outlays	345	594	682	776	878
Net Changes in User Fees:					
Estimated Authorization Level	0	0	0	0	0
Estimated Outlays	−179	−8	−11	−13	−86
Other Proposed Changes:					
Risk Evaluation and Mitigation Strategies:					
Authorization Level	80	80	80	80	80
Estimated Outlays	56	79	84	81	81
Provisions Affecting Pediatric Populations:					
Program for Pediatric Research:					
Estimated Authorization Level	0	75	150	200	225
Estimated Outlays	0	19	79	144	190
Other Provisions:					
Estimated Authorization Level	14	19	24	25	26
Estimated Outlays	11	19	23	25	26
Other Provisions[1]:					
Estimated Authorization Level	15	21	25	27	28
Estimated Outlays	12	20	22	26	28
Total Changes:					
Estimated Authorization Level	109	195	279	332	359

TABLE 1. ESTIMATED IMPACT OF H.R. 2900 ON DISCRETIONARY SPENDING—Continued

	By fiscal year, in millions of dollars—				
	2008	2009	2010	2011	2012
Estimated Outlays	−100	129	197	263	239

[1]Amounts primarily reflect costs for the Food and Drug Administration and the National Institutes of Health of expanding federal efforts to collect information on clinical trials, establishing partnerships with private entities to foster the innovation and safety of medical products, and enhancing federal oversight of medical devices to assess their safety after market entry.

TABLE 2. CHANGES IN DIRECT SPENDING AND REVENUES UNDER H.R. 2900

	By fiscal year, in millions of dollars—											
	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2008–2012	2008–2017
CHANGES IN DIRECT SPENDING												
Estimated Budget Authority	0	*	*	1	5	11	19	29	53	83	7	200
Estimated Outlays	0	*	*	1	5	11	19	29	53	83	7	200
CHANGES IN REVENUES												
Estimated Revenues:												
On-budget	0	*	*	*	−1	−2	−3	−4	−7	−11	−1	−28
Off-budget	0	*	*	*	*	−1	−1	−2	−4	−5	*	−13
Total	0	*	*	*	−1	−3	−4	−6	−11	−16	−1	−41

Note: * = less than $500,000; components may not sum to totals because of rounding.

FEDERAL MANDATES STATEMENT

The Committee adopts as its own the estimate of Federal mandates prepared by the Director of the Congressional Budget Office pursuant to section 423 of the Unfunded Mandates Reform Act.

ADVISORY COMMITTEE STATEMENT

Regarding section 5(b) of the Federal Advisory Committee Act, section 901(d)(4) of the bill amends section 303 of the Federal Food, Drug, and Cosmetic Act to add a subsection (g) (relating to civil money penalties) that, in paragraph (7), requires the establishment of an advisory committee to provide certain advice to the Secretary of Health and Human Services regarding direct-to-consumer advertising. The Committee finds that establishing the advisory committee is the most efficient way of carrying out the policies involved.

CONSTITUTIONAL AUTHORITY STATEMENT

Pursuant to clause 3(d)(1) of rule XIII of the Rules of the House of Representatives, the Committee finds that the Constitutional authority for this legislation is provided in Article I, section 8, clause 3, which grants Congress the power to regulate commerce with foreign nations, among the several States, and with the Indian tribes, and in the provisions of Article I, section 8, clause 1, that relate to expending funds to provide for the general welfare of the United States.

APPLICABILITY TO LEGISLATIVE BRANCH

The Committee finds that the legislation does not relate to the terms and conditions of employment or access to public services or accommodations within the meaning of section 102(b)(3) of the Congressional Accountability Act.

SECTION-BY-SECTION ANALYSIS OF THE LEGISLATION

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

Sec. 1. Short title.
Sec. 2. Table of contents.

TITLE I—PRESCRIPTION DRUG USER FEE AMENDMENTS OF 2007

Sec. 101. Short title; references in title.
Sec. 102. Definitions.
Sec. 103. Authority to assess and use drug fees.
Sec. 104. Fees relating to advisory review of prescription-drug television advertising.
Sec. 105. Reauthorization; reporting requirements.
Sec. 106. Sunset dates.

TITLE II—MEDICAL DEVICE USER FEE AMENDMENTS OF 2007

Sec. 201. Short title; references in title.

Subtitle A—Fees Related to Medical Devices

Sec. 211. Definitions.
Sec. 212. Authority to assess and use device fees.
Sec. 213. Annual reports.
Sec. 214. Consultation.
Sec. 215. Additional authorization of appropriations for postmarket safety information.
Sec. 216. Effective date.
Sec. 217. Sunset clause.

Subtitle B—Amendments Regarding Regulation of Medical Devices

Sec. 221. Extension of authority for third party review of premarket notification.
Sec. 222. Registration.
Sec. 223. Filing of lists of drugs and devices manufactured, prepared, propagated, and compounded by registrants; statements; accompanying disclosures.
Sec. 224. Electronic registration and listing.
Sec. 225. Report by Government Accountability Office.
Sec. 226. Unique device identification system.
Sec. 227. Frequency of reporting for certain devices.
Sec. 228. Inspections by accredited persons.
Sec. 229. Study of nosocomial infections relating to medical devices.

TITLE III—PEDIATRIC MEDICAL DEVICE SAFETY AND IMPROVEMENT ACT

Sec. 301. Short title.
Sec. 302. Tracking pediatric device approvals.
Sec. 303. Modification to humanitarian device exemption.
Sec. 304. Encouraging pediatric medical device research.
Sec. 305. Demonstration grants for improving pediatric device availability.
Sec. 306. Amendments to office of pediatric therapeutics and pediatric advisory committee.
Sec. 307. Postmarket Studies.

TITLE IV—PEDIATRIC RESEARCH EQUITY ACT OF 2007

Sec. 401. Short title.
Sec. 402. Reauthorization of Pediatric Research Equity Act.
Sec. 403. Government Accountability Office report.

TITLE V—BEST PHARMACEUTICALS FOR CHILDREN ACT OF 2007

Sec. 501. Short title.
Sec. 502. Reauthorization of Best Pharmaceuticals for Children Act.

TITLE VI—REAGAN-UDALL FOUNDATION

Sec. 601. The Reagan-Udall Foundation for the Food and Drug Administration.
Sec. 602. Office of the Chief Scientist.
Sec. 603. Critical path public-private partnerships.

TITLE VII—CONFLICTS OF INTEREST

Sec. 701. Conflicts of interest.

TITLE VIII—CLINICAL TRIAL DATABASES

Sec. 801. Clinical trial registry database and clinical trial results database.
Sec. 802. Study by Government Accountability Office.

TITLE IX—RISK EVALUATION AND MITIGATION STRATEGIES

Sec. 901. Postmarket studies and clinical trials regarding human drugs; risk evaluation and mitigation strategies.
Sec. 902. Enforcement.
Sec. 903. No effect on withdrawal or suspension of approval.
Sec. 904. Benefit-risk assessments.
Sec. 905. Postmarket risk identification and analysis system for active surveillance and assessment.
Sec. 907. Statement for inclusion in direct-to-consumer advertisements of drugs.
Sec. 908. Clinical trial guidance for antibiotic drugs.
Sec. 909. Prohibition against food to which drugs or biological products have been added.
Sec. 910. Assuring pharmaceutical safety.
Sec. 911. Orphan antibiotic drugs.
Sec. 912. Authorization of appropriations.
Sec. 913. Effective date and applicability.

TITLE I—PRESCRIPTION DRUG USER FEE AMENDMENTS OF 2007

Section 101. Short title; references in act

Section 101 establishes the short title as the "Prescription Drug User Fee Amendments of 2007". This section also establishes that

references in the Act are to the Federal Food, Drug, and Cosmetic Act (FFDCA).

Section 102. Definitions

Section 102 amends Section 735 of the Federal Food, Drug, and Cosmetic Act to eliminate the distinction between approvals under 505(b)(1) and 505(b)(2) for requirements of this section. This section also expands the definition of postmarket safety activities beyond "collecting, developing, and reviewing safety information on the drugs, including adverse event reports. . ." The new definition includes the development and use of improved adverse-event data-collection systems, including information technology systems and analytical tools to assess potential safety problems, including access to external data bases. The definition also includes a summary analysis of adverse drug reaction reports received for recently approved drugs, regular bi-weekly screening of the Adverse Event Reporting System, updating Adverse Event Reporting System reports every six months, and reporting to Congress on the recommendations received on postmarket safety activities.

Section 102 amends Section 735 of the FFDCA to eliminate the three-year limit on use of fees for postmarket safety activities, substitute appropriate year references, and expand the definition of the term "person" to include "an affiliate thereof."

Section 103. Authority to assess and use drug fees

Types of Fees. Section 103 amends Section 736 "Authority to Assess and Use Drug Fees" of the FFDCA. Subsection 736(a) "Types of Fees" is amended to clarify that the Secretary of Health and Human Services will retain 25 percent of the application fees for applications that are withdrawn before filing; and that applications or supplements previously refused for filing or that were withdrawn before filing will be subject to the full user fee upon being resubmitted or filed over protest, unless otherwise exempted or waived.

Special Rules for Positron Emission Tomography Drugs. Section 103 provides special rules for positron emission tomography (PET) drugs to be exempt from the annual establishment fee. An applicant that is a not-for-profit medical center that has only one establishment for the production of PET drugs, and at least 95 percent of the doses produced by such establishment will be used within the medical center may be exempt from the annual establishment fee. Any other person named as an applicant would pay one-sixth of the annual establishment fee.

Fee Revenue Amounts. Section 103 amends subsection 736(b) "Fee Revenue Amounts" to establish fees that, for each of FY2008 through FY2012, generate total annual revenue of $392,783,000, plus an adjustment for FY2007 workload. The workload adjustment factor is modified for FY2007 to apply to the FY2008 total. Each subsequent fiscal year will be determined based on the adjusted FY2008 total increased by the specified amount for each year, adjusted according to changes in the total annual appropriation for FDA relative to the appropriation for FY2007. Total revenue will continue to be equally divided among application fees, establishment fees, and product fees. An additional $225,000,000 in fee revenue is provided for drug safety activities. This amount will be trig-

gered by appropriations amounts. There will be a dollar-for-dollar decrease in user fees collected for postmarket safety for every dollar appropriated for the same purpose.

Adjustments to Fees. Section 103 amends subsection 736(c) "Adjustments to Fees" to modify the inflation adjustment for the annual statutory revenue target to account for changes in personnel compensation and benefits costs. The workload adjustment regarding commercial investigational new drug applications (INDs) is modified to use the number of active, rather than new, commercial INDs submitted each year. A 2 percent ceiling is set on total workload adjustment due to changes in review activities, and the Secretary is required to contract with an independent accounting firm to study the FY2009 adjustments and make recommendations for changing the adjustment methodology.

The rent and rent-related cost adjustment is modified beginning in FY2010 to decrease the total fee revenue amount up to $11,721,000 for a fiscal year if actual costs paid for rent and rent-related expenses in the preceding fiscal year were less than had been estimated.

Fee Waiver or Reduction. Section 103 amends subsection 736(d) "Fee Waiver or Reduction" to add to the definition of a small business (500-mployee maximum) that the business have no approved drug product already in interstate commerce. The Secretary is also required to consider only the circumstances and assets of the applicant (and affiliates of the applicant) in determining whether to grant a waiver or fee reduction.

Crediting and Availability of Fees. Section 103 amends subsection 736(e) "Crediting and Availability of Fees" to authorize appropriations for each of fiscal years 2008 through 2012 an amount equal to the total revenue amount. If the fees to be collected exceed the cumulative amount appropriated for fees, the excess will be credited to the appropriation account of FDA and subtracted from the amount of fees authorized.

Exemption for Orphan Drugs. Section 103 further amends section 736 to exempt orphan drugs from product and facility fees. The orphan drug must have had sales in the United States in the previous year of less than $25,000,000, meet public health requirements, and must be owned or licensed and marketed by a company that had less than $100,000,000 in gross worldwide revenue.

Section 104. Fees relating to advisory review of prescription-drug television advertising

Section 104 amends part 2 of subchapter C of chapter VII by adding after section 736 the following:

> *"Section 736A. Fees Relating to Advisory Review of Prescription-Drug Television Advertising."*

New section 736A establishes a new user fee program to authorize FDA to assess, collect, and use fees for the advisory review of proposed direct-to-consumer (DTC) television advertisements prior to their initial release. To the extent there are additional staff resources available under this program that are not necessary for advisory reviews of DTC television advertisements, the fees may be used for advisory comments on other proposed ads and promotional material prior to public dissemination.

New section 736A establishes an advisory review fee for each advertisement a company submits to FDA with a request for an advisory review and a one-time operating reserve fee the first time a company pays an advisory review fee.

New section 736A specifies requirements for notices and late payments on submissions; allows for no waivers, exemptions, or reductions; and allows for no refunds, unless the Secretary has received less than $11,250,000 during the first 120 days after enactment, in which case the program shall terminate and all fees be refunded.

New section 736A specifies revenue at $6,250,000 per year (FY2008 through FY2012), with inflation, personnel cost, and workload adjustments. Methodologies and ceilings are provided for setting fees. Additional provisions restrict the use of fee revenue, provide for the termination of the program if inadequate fees have been collected, and outline procedures in the event of a company's failure to pay or the inadequate funding of the program.

New section 736A authorizes to be appropriated for fees, for each of FY2008 through FY2012, the total revenue amount plus adjustments, and any amount necessary for ending the program at the end of FY2012, or earlier, if funding of the program is inadequate.

Section 105. Reauthorization; reporting requirements

The fees authorized by this Title will be dedicated towards expediting the drug development process and review process as set forth in the goals identified for purposes of part 2 of subchapter C of chapter VII of the Federal Food, Drug, and Cosmetic Act, in the letters from the Secretary of Health and Human Services to the Chairman of the Committee on Energy and Commerce of the House of Representatives and the Chairman of the Committee on Health, Education, Labor and Pensions of the Senate, as set forth in the Congressional Record.

Section 105 requires that the Secretary submit to Congress annually a performance report to cover FDA's progress in achieving the goals identified in letters from the Secretary to the authorizing committees. The Secretary is also required to submit to Congress an annual fiscal report describing the implementation of authority for advertising fees and FDA's use of such fees.

Section 105 outlines the process the Secretary must follow in developing recommendations to Congress regarding goals for the next reauthorization. The Secretary is required to: (1) consult with the authorizing committees, scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry; (2) publish recommendations in the Federal Register after negotiations with regulated industry and patient and consumer advocacy groups; (3) provide a comment period regarding these recommendations, hold a public meeting, and revise the recommendations as necessary; and (4) transmit the revised recommendations to Congress by January 15, 2012, along with a summary of the public views and comments and any changes made to the recommendations in response.

Section 106. Sunset dates

Section 106 sets October 1, 2012, for the sunset of sections 102 (definitions), 103 (the authority to assess and use drug fees), and

104 (the authority to assess and use prescription drug advertising fees).

TITLE II—MEDICAL DEVICE USER FEE AMENDMENTS OF 2007

Section 201. Short title; references

Section 201 establishes the short title as the "Medical Device User Fee Amendments of 2007". This section also establishes that references in the Act are to the Federal Food, Drug, and Cosmetic Act (FFDCA).

Subtitle A—Fees Related to Medical Devices

Section 211. Definitions

Section 211 adds or amends several definitions in section 737 of the FFDCA applicable to medical device fees. Newly added definitions for 30-day notice, request for classification information, annual fee, and establishment subject to regulation (and under the last of these, descriptions of manufacturer, single-use device reprocessor, and specification developer), reflect the addition of new types of fees. The addition of a definition for person specifies that the term includes an affiliate thereof. A change in the definition of adjustment factor shifts from April to October the Consumer Price Index numbers used as the basis for calculating the amount of direct medical device related appropriations necessary to enable FDA to collect medical device user fees.

Section 212. Authority to assess and use device fees

Types of Fees, Fee Amounts, and Exceptions. Section 212 adds three new types of fees including: (1) an annual establishment registration fee (paid once each year by each manufacturer), (2) an annual fee for filing periodic reports (generally applicable to Class III devices—those requiring FDA's highest level of safety controls), and (3) a fee for 30-Day Notices (submitted for modifications to manufacturing processes or methods—typically only required for Class III devices). Other types of fees required by the FFDCA would remain in place.

Section 212 decreases fee amounts. This section also strikes a provision that enables the Secretary of the Department of Health and Human Services to adjust the premarket notification fee amount annually so that, in aggregate, these fees comprise a target amount. No other fee amounts are set by this method.

Section 212 contains an exception to new annual establishment registration fees for State and Federal governmental entities, and Indian Tribes (as defined in the Indian Self Determination and Educational Assistance Act).

Section 212 provides that, once the new fees are set for 2008, they will generally increase each year by 8.5 percent. For the newly created establishment fee, the Secretary could increase the fee amount in FY2010, up to 8.5 percent over the annual rate of increase, if fewer than 12,250 establishments paid the fee in FY2009.

Payment and Refunds. Section 212 updates the payment information section to reflect new fee types and dates. It also adds a provision to current law, which enables the Secretary to refund portions of fees for modular applications withdrawn before FDA takes its first action, or before other subsequent submissions are

made. For all types of applications, current law allows for partial refunds for applications refused for filing or withdrawn before filing, and for partial or full refunds for applications withdrawn before FDA takes its first action.

Fees for Small Businesses. Section 212 makes it easier to qualify as a small business, removing a requirement that the assets of partners and parent firms be considered. This section also enables foreign businesses to qualify as small businesses by allowing evidence of income from sources other than the Federal income tax return submitted to the Internal Revenue Service. In addition, section 212 would further reduce the application fees paid by small business.

Effect of Failure to Pay Fees. Section 212 expands the provision in current law that specifies that the Secretary shall deem incomplete an application from a person with a missing fee and shall not accept it until all fees owed by the person are paid to encompass the new application fees. This section also prevents the Secretary from considering complete and accepting registration information submitted under FFDCA §510 (Registration of Producers of Drugs and Devices) until the registration fee is paid.

Conditions and Authority. Section 212 extends, for each subsequent year, the provision in current law that specifies that fees may not be assessed and the Secretary is not expected to meet any performance goals if the amount of medical device-related direct appropriations falls below a specified threshold ($205,720,000 multiplied by an annual adjustment factor).

Section 212 extends the provision that states if the Secretary is prevented from collecting fees during any portion of a fiscal year because of insufficient direct appropriations, he may collect them later during that fiscal year without any modification in the rate to include the newly added fees as well.

Crediting and Availability of Fees. Section 212 authorizes appropriations for FY2008—FY2012 in the following amounts: $48,431,000 for FY2008; $52,547,000 for FY2009; $57,014,000 for FY2010; $61,860,000 for FY2011; and $67,118,000 for FY2012.

Section 212 allows FDA to aggregate all fees collected between FY2008 and FY2011 and compare that amount to the aggregate amount authorized for the same period. A reduction would be made in fees in the final year only if the amount collected in the four-year period exceeded the amount authorized for the same period.

Section 213. Annual reports

Section 213 requires the Secretary to submit annual progress reports to relevant congressional committees regarding FDA's progress in achieving fee-related performance goals specified in a letter from the Secretary, and regarding the implementation of the authority to collect such fees. This section also specifies that the implementation report should include a description of the use of such fees for postmarket safety activities.

Section 214. Consultation

Section 214 outlines the process the Secretary must follow in developing recommendations to Congress regarding goals for the next reauthorization. The Secretary is required to: (1) consult with the authorizing committees, scientific and academic experts, healthcare

professionals, representatives of patient and consumer advocacy groups, and the regulated industry; (2) publish those developed recommendations in the Federal Register; and (3) provide a comment period.

Section 215. Additional authorization of appropriations for postmarket safety information

Section 215 authorizes additional appropriations for FY2008–FY2012 of $7,100,000 for the purpose of collecting, developing, reviewing, and evaluating postmarket safety information on medical devices.

Section 216. Effective date

Section 216 states that the amendments made by this Act shall take effect on the date of enactment of the Act, except fees shall be assessed for all premarket submissions received on or after October 1, 2007, regardless of the date of enactment.

Section 217. Sunset clause

Section 217 states that user fee amendments would cease to be effective on October 1, 2012, except that the section regarding annual reports would cease to be effective on January 31, 2013.

Subtitle B—Amendments Regarding Regulation of Medical Devices

Section 221. Extension of authority for third-party review of premarket notifications

Section 221 extends the authority of the third-party review of premarket notifications through October 1, 2012.

Section 222. Registration

Section 222 restricts the registration period for producers of devices to the period of October 1–December 31 of each year.

Section 223. Section filing lists of drugs, and devices manufactured, prepared, propagated, and compounded by registrants; statements and accompanying disclosures

Section 223 changes the timing for those involved with devices, to provide a list of drugs and devices on which they perform specific functions, such as manufacturing and compounding to once per year between October 1 and December 31, thus eliminating the requirement to file a second list each year.

Section 224. Electronic registration and listing

Current law requires registrations to be submitted to the Secretary by electronic means, upon a finding by the Secretary that the electronic receipt of such registrations is feasible, unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver (FFDCA § 510(p)). Section 224 adds the requirement that information required by the section be submitted electronically unless the Secretary grants a waiver because electronic registration is not reasonable for the person requesting such a waiver.

Section 225. Report by Government Accountability Office

Section 225 requires the Comptroller General to conduct a study to determine the safety and effectiveness of a new device based on the criteria set forth by the Secretary's evaluation of the device and submit a report to Congress on his findings within one year of the study.

Section 226. Unique device identification system

Section 226 requires the Secretary to establish a unique identification system for medical devices.

Section 227. Frequency of reporting for unique devices

Section 227 allows device manufacturer to submit reports on a quarterly basis in a summary form, except for devices that are life supporting or life sustaining, which can be submitted according to part 803 of Code 21.

Section 228. Inspections by accredited persons

Section 228 requires the device inspector to notify the Secretary of any withdrawal, suspension, restriction, or expiration of certificate of conformance within 30 days of such change.

Before the inspection, the owner of the device must submit to the Secretary a notice providing the date of the last inspection, a statement declaring the intention of having an accredited inspector, a statement identifying the intended inspector, and a certification that at least one device is marketed in the United States and is intended to be marketed in at least one foreign country where the accredited inspector is certified.

The Secretary may deny clearance or ask for additional information such as compliance data or disclosure of the relationship between the manufacturer and the inspector. The manufacturer must respond within 60 days of the Secretary's request for additional information. If the Secretary denies clearance of an accredited inspector, the owner may make a new selection. At the Secretary's discretion, the manufacturer may submit audits assessing conformance with appropriate quality system standards.

Section 229. Study of nosocomial infections related to medical devices

Section 229 requires the Comptroller General to submit a report on nosocomial infections attributed to medical devices and the causes of such infections and report to Congress on his findings no later than one year after enactment of this law. Nosocomial infection is defined as an infection that is acquired while a person is a patient of a hospital and was not present or incubating before the patient received treatment at that hospital.

TITLE III—PEDIATRIC MEDICAL DEVICE SAFETY AND IMPROVEMENT ACT OF 2007

Section 301. Short title

Section 301 establishes the short title as the "Pediatric Medical Device Safety and Improvement Act of 2007".

Section 302. Tracking Pediatric Device Approvals

Section 302 amends chapter V of the Federal Food, Drug, and Cosmetic Act (FFDCA) by inserting a new section 515A "Pediatric Uses of Devices".

"Section 515A. Pediatric Uses of Devices."

New section 515A requires that an application or protocol submitted to the Secretary for a device must include a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure, and the number of affected pediatric patients.

New section 515A creates a mechanism to allow FDA to track the number and types of devices approved specifically for children or for conditions that occur in children, as well as the approval times for premarket approvals and humanitarian device exemptions. The Secretary shall submit a report to Congress on the results 18 months after enactment. FDA is granted specific authority to allow the extrapolation of adult data to support a pediatric indication, as appropriate.

Section 303. Modification to humanitarian device exemption (HDE)

Section 303 amends section 520(m) of the FFDCA to modify the existing HDE provision to allow profit for devices specifically designed to meet a pediatric need. This provision applies from the date of enactment of this section. To prevent abuse, this section reverts to current law (no profit) on sales that exceed the number estimated to be needed for the approved condition (modeled after existing Orphan Products Division designation process). Under no circumstances can there be a profit on sales if the device is used to treat or diagnose diseases or conditions affecting more than 4,000 individuals in the U.S. per year (same as current law). Upon the date of enactment of this section, already approved adult HDEs shall be eligible for the HDE profit modification if they meet the conditions of the section.

Section 303 defines pediatric patients as patients who are 21 years of age or younger at the time of diagnosis or treatment and defines pediatric subpopulation as neonates, infants, children, and adolescents. As a check on postmarket safety, this section requires adverse events for pediatric HDE devices to be reported to the Office of Pediatric Therapeutics and requires the Pediatric Advisory Committee to conduct an annual review to determine whether the exemption is still appropriate.

Section 303 requires a Comptroller General report no later than January 1, 2012, to assess whether the HDE profit exemption has increased the availability of pediatric devices, what its impact is on premarket approvals, conditions or diseases the pediatric devices were intended to treat or diagnose, costs of the pediatric devices and the extent to which those costs are covered by insurance, profits made by manufacturers for each device that receives an exemption, existing obstacles to pediatric device development, and an evaluation of the demonstration grants under Section 305.

Section 303 directs FDA to issue guidance to institutional review committees for responding to HDEs.

Section 304. Encouraging pediatric medical device research

Section 304 requires the National Institutes of Health (NIH) to designate a "contact point" to help innovators access existing funding for pediatric medical device development. NIH, FDA, and the Agency for Healthcare Research and Quality (AHRQ) shall submit a plan, within 180 days of enactment, for pediatric medical device research that identifies gaps and proposes a research agenda for addressing them. As needed, the plan can include a survey of pediatric medical providers to identify unmet pediatric medical device needs.

Section 305. Demonstration grants for improving pediatric device availability

Section 305 establishes demonstration grants for non-profit consortia to promote pediatric device development, including "matchmaking" between inventors and manufacturers and federal resources and mentoring and project management throughout the development process. The consortia must coordinate with NIH to identify research issues that require further study and with the FDA to facilitate approval of pediatric indications. H.R. 2900 authorizes an appropriation of $6,000,000 for each of FY2007–FY2011 for these grants.

Section 306. Amendments to Office of Pediatric Therapeutics and Pediatric Advisory Committee

Section 306 amends section 14 of the Best Pharmaceuticals for Children Act to grant explicit authority to FDA's Pediatric Advisory Committee to monitor pediatric devices and make recommendations for improving their availability and safety.

Section 307. Postmarket studies

Section 307 amends section 522 of the FFDCA to allow FDA to require postmarket studies as a condition of clearance for the categories of devices found in this section. This includes "a class II or class III device the failure of which would be reasonably likely to have serious adverse health consequences or is intended to be (1) implanted in the human body for more than one year, or (2) a life sustaining or life supporting device used outside a device user facility." This also includes devices intended for use in pediatric patients, or intended for use generally, but expected to have significant use by pediatric patients. This provision ensures that the Secretary can require postmarket surveillance not only for those devices specifically intended for pediatric uses, but also for devices that are cleared without specifying a specific patient group, yet are expected to be used to a significant degree in pediatric patients. Requiring postmarket surveillance for this latter group of devices reflects the Committee's understanding that most devices that FDA reviews do not specify whether a device is for an adult or child; they are reviewed for indications for use in all populations for whom the use is applicable. Postmarket surveillance for these devices in pediatric patients utilizes collection of data in a subpopulation of a larger population for whom the device is intended.

Section 307 grants FDA the ability to require studies longer than three years with respect to a device that is to have significant use in pediatric populations, if such studies would be necessary to ad-

dress longer-term pediatric questions, such as the impact on growth and development.

Section 307 establishes a dispute resolution process for any order or condition requiring postmarket surveillance under this section. During this process, the device may not be deemed misbranded unless it is necessary to protect the public health.

While children and adults suffer from many of the same diseases and conditions, their device needs can vary considerably due to differences in size, rates of growth, critical development periods, anatomy (e.g., organ size), physiological differences (e.g., breathing and heart rates), physical activity levels, etc. In addition, since there are many pediatric diseases for which no adult parallel exists, in some cases devices exclusively designed for children are needed.

The Committee believes that, like adults, children deserve medical devices that are safe, effective, and designed for their particular needs. Yet, to date, because the pediatric market is so small and pediatric diseases are relatively rare, there has been little incentive for the development of devices specifically designed for children. Typically, pediatric providers must resort to "jury-rigging" or fashioning makeshift device solutions for pediatric use. When that is not an option, providers may be forced to use more invasive treatment or less effective therapies.

In an effort to gain more information about pediatric uses of devices, the legislation amends section 522 to give the Secretary new authority to require postmarket surveillance as a condition of approval or clearance. This change is consistent with recommendations of the Institute of Medicine. This new authority applies to class II and class III devices whether approved under section 515 or cleared under section 510(k). In addition, this authority applies to devices either intended for use in pediatric patients or not labeled for pediatric use, but nonetheless expected to have significant use in pediatric populations. The provision of authority to require postmarket surveillance for this latter group of devices reflects the Committee's understanding that most devices are for general use and some devices may be labeled only for adult use—but both of these types of devices may still be expected to have significant use in children. The Committee intends this new authority to be available to the Secretary when appropriate, as discussed below.

This provision will ensure that FDA has authority to gather information about physicians' uses of devices in pediatric populations in the post-market setting whether or not the device is labeled for pediatric use. Safety and effectiveness data to support a pediatric use is most appropriately collected in the premarket setting in accordance with the Agency's investigational device exemption and human subject protection regulations. The authority to require collection of postmarket safety data on device use in pediatric populations is not intended to replace this important premarket process. The Committee does not intend to encourage or legitimize any promotion of an unapproved and unproven use of a device in pediatric patients.

An order under section 522 directing post-market surveillance on pediatric use of a device shall not be construed to permit any promotion, sale, or distribution that is otherwise prohibited by law. This provision should not be seen to encourage any promotion of off-label pediatric uses of devices that have been cleared or ap-

proved for adult use but for which there is no or limited safety and effectiveness data concerning uses in children.

The Committee encourages the Secretary to require postmarket surveillance, where appropriate. The Committee understands that legitimate circumstances may arise that result in questions about a postmarket surveillance order, requiring a means of appealing the order. Because of the types of questions that likely will result in appeals, the Committee believes that the already established dispute resolution process for addressing scientific controversies under Section 562 provides the best means of determining the appropriateness of a post-market surveillance order. Importantly, to avoid adverse impact to the public health through a product's withdrawal, the Committee provides that during the pendency of an appeal of a postmarket surveillance order, the Secretary shall not consider a device to be misbranded or otherwise in violation of such order or a related requirement of this Act, unless the Secretary determines it is necessary to protect the public health. While the exercise of this authority likely will be rare, it is essential that the Secretary retain the discretion to act in the event that such action is necessary to protect the public health.

TITLE IV—PEDIATRIC RESEARCH EQUITY ACT OF 2007

Section 402. Reauthorization of the Pediatric Research Equity Act

Section 402 amends subsection 505B of the FFDCA in the following ways:

> *"Section 505B. Research into Pediatric Uses for Drugs and Biological Products."*

New Drugs and Biological Products. New section 505B provides that the Secretary may require the sponsor of an application for a drug or a license for a biological product to submit an assessment of the effect of their product in pediatric populations. The assessment must include the safety and effectiveness of the drug or biological product for the claimed indications in all relevant pediatric subpopulations and must support dosing and administration for each pediatric subpopulation.

If the course of disease and the effects of the drug are similar in adult and child patients, the Secretary may conclude that effectiveness in pediatric populations can be extrapolated from studies of adults. Extrapolation may also be used between age groups. Scientific data supporting extrapolation must be included in any pertinent reviews for the application for drugs and biologics.

New section 505B states that the Secretary may defer submission of some or all pediatric assessments until after approval of a drug or issuance of a license for a biological product. If submission is deferred, the applicant must submit an annual report to the Secretary including information detailing the progress made in conducting pediatric studies, and if no progress is made, evidence that such studies will be conducted with due diligence. These reports shall be made available to the public in an easily accessible manner.

New section 505B states that the Secretary may grant a full waiver of pediatric assessments if the necessary studies are impossible or highly impracticable, there is evidence that the product

would be ineffective or unsafe in pediatric populations, or the product does not represent a meaningful therapeutic benefit and will not be used in a substantial number of pediatric patients. The Secretary may also issue a partial waiver. Companies seeking waivers on the grounds that a pediatric formulation cannot be developed must submit documentation detailing why a pediatric formulation cannot be developed. If a full or partial waiver is granted, the reason for the waiver must be included in the product labeling.

Marketed Drugs and Biological Products. New section 505B states that the Secretary may require the sponsor or the holder of an approved application for a drug or a license for a biological product to submit by a specified date an assessment of the effect of their product in pediatric populations.

New section 505B states that the Secretary may grant a full waiver if the necessary studies are impossible or highly impracticable, there is evidence that the product would be ineffective or unsafe in pediatric populations, or the product does not represent a meaningful therapeutic benefit and will not be used in a substantial number of pediatric patients. The Secretary may also issue a partial waiver. Companies seeking waivers on the grounds that a pediatric formulation cannot be developed must submit documentation detailing why a pediatric formulation cannot be developed. If a full or partial waiver is granted, the reason for the waiver must be included in the product labeling.

Meaningful Therapeutic Benefit. New section 505B outlines the criteria used to determine if a product provides a meaningful therapeutic benefit.

Submission of Assessments. New section 505B states that if a person fails to submit an assessment or a request for approval of a pediatric formulation, the drug or biological product may be deemed misbranded. Failure to submit the assessment or request, however, cannot be the basis for withdrawing approval of the product or revoking the license of the product.

Meetings. New section 505B states that the Secretary shall meet with the sponsor of a new drug or biological product before and during the investigational process to discuss the sponsor's plans and timelines for pediatric studies and any planned request by the sponsor for waiver or deferral of pediatric studies.

Review of Pediatric Plans, Deferrals, and Waivers. New section 505B states that the Secretary shall establish an internal review committee, composed of employees with expertise in pediatrics and other subspecialties, to review all pediatric plans, deferrals, and waivers made under this section. The Secretary is required to track the number and types of assessments, deferrals, waivers, and labeling changes conducted under this section, as well as the number of pediatric formulations developed or not developed and an annual summary of information submitted for deferrals.

Labeling Changes. New section 505B considers applications or supplements proposing a labeling change as a result of pediatric studies under PREA a priority application or supplement.

If label changes are not made within 180 days of submission of the application, a dispute resolution process is outlined. If an application sponsor does not agree with the Commissioner's request for label change within 30 days, the matter is referred to the Pediatric Advisory Committee. The Committee shall consider the matter

within 90 days and make recommendations to the Commissioner. The Commissioner then has 30 days to make a request to the sponsor of the application to make any labeling changes. If the sponsor still does not agree with the recommendations, the Commissioner may deem the drug misbranded.

New section 505B grants the Secretary the authority to order the label of a product to include information from studies indicating that a drug is or is not safe and effective in pediatric populations or subpopulations, including whether the study results are inconclusive.

Dissemination of Pediatric Information. New section 505B requires the Secretary to make medical, statistical, and clinical pharmacology reviews of pediatric studies available to the public not later than 180 days after the date of submission of a report. The Secretary will also require the sponsors of studies that result in labeling changes reflected in the annual summary to distribute this information to physicians and other healthcare providers.

Adverse Event Reporting. New section 505B requires the Secretary, during the one-year period beginning on the date a labeling change is made, to ensure that all adverse event reports that have been received for a drug are referred to the Office of Pediatric Therapeutics and provided for review by the Pediatric Advisory Committee.

Following the one year period, the Secretary is required to provide the Office of Pediatric Therapeutics a report of any information regarding pediatric adverse events for a drug for which a pediatric study was conducted. When considering the report, the director of the Office of Pediatric Therapeutics may provide for the review of the report by the Pediatric Advisory Committee including obtaining any committee recommendations regarding whether the Secretary should take action.

Scope of Authority. New section 505B states that the Secretary may not require pediatric assessment of a drug or biological product outside of what is described in this section.

Orphan Drugs. New section 505B does not apply to orphan drugs unless required otherwise by the Secretary.

Institute of Medicine Study. New section 505B requires the Secretary to ask IOM to conduct a study of the implementation of PREA and report to Congress not later than three years after enactment of this section. The study shall review and assess pediatric studies conducted since 1997 and the use of extrapolation for pediatric subpopulations, the use of alternative endpoints, neonatal assessment tools, the number and type of pediatric adverse events, and ethical issues in pediatric clinical trials.

Section 403. Government Accountability Office Report

Section 403 provides that no later than September 1, 2011, the Comptroller General of the U.S., in consultation with the Secretary, shall submit to Congress a report that addresses the effectiveness of sections 505A and 505B of the FFDCA and section 409I of the PHSA in ensuring that medicines used by children are tested and properly labeled.

TITLE V—BEST PHARMACEUTICALS FOR CHILDREN ACT

Section 501. Short title

Section 501 establishes the short title as the "Best Pharmaceuticals for Children Act of 2007".

Section 502. Reauthorization of the Best Pharmaceuticals for Children Act

Section 502 amends section 505A of the Federal Food, Drug, and Cosmetic Act to read as follows:

"Section 505A. Pediatric Studies of Drugs."

Definitions. New section 505A amends the definition of pediatric studies to include preclinical studies.

Market Exclusivity for New Drugs. New section 505A states that if, prior to the approval of a new drug application, the Secretary determines that the new drug may produce health benefits in the pediatric population, the Secretary may make a written request to the holder of an approved drug application to conduct pediatric studies. Should the holder agree to the request, complete the appropriate studies in the designated timeframe, provide reports, and comply with labeling changes requested by the Secretary, the Secretary may grant six months of additional market exclusivity. The Secretary shall not grant additional market exclusivity for a new drug if the determination is made within one year before either the last listed patent for that product has expired or all other exclusivities have expired, whichever is later.

Market Exclusivity for Already Marketed Drugs. New section 505A states that if the Secretary discovers that an already marketed drug may produce health benefits in the pediatric population, the Secretary may make a written request to the holder of an approved drug application to conduct pediatric studies. Should the holder agree to the request, completes the appropriate studies in the designated timeframe, provide reports, and comply with labeling changes requested by the Secretary, the Secretary may grant six months of additional market exclusivity. The Secretary shall not grant additional market exclusivity if the determination is made within the final year of the patent life.

Conduct of Pediatric Studies. New section 505A grants the Secretary the authority to issue a written request for conduct of pediatric studies. In issuing a request, the Secretary must take into account adequate representation of children of ethnic and racial minorities. The request must be in writing, include a timeframe for the study requested, and request that the sponsor propose pediatric labeling resulting from the study. The Secretary may issue a single written request that may relate to more than one use of a drug, including approved and unapproved uses.

The sponsor has 180 days to accept or decline a written request for pediatric studies. If the sponsor does not agree to the request the sponsor shall state its reasons for declining the study. If the reason the sponsor declined the written request is because a pediatric formulation is not possible, the sponsor must state why a formulation cannot be developed. Sponsors agreeing to complete studies are required to submit all postmarket adverse event reports regarding the drug when the sponsor submits its report. The Sec-

retary is required to accept or reject the study reports within 180 days after the sponsor's submission.

Notice of Determinations on Studies Requirement. New section 505A requires the Secretary to publish a notice of determination within 30 days after the date of the Secretary's determination regarding market exclusivity. The Secretary is also required to publish a notice identifying any drug for which a pediatric formulation was developed, studied, and found to be safe and effective in the pediatric population if the pediatric formulation is not introduced to the market within one year of the date that the notice is published. The Secretary must publish this no later than 30 days after the expiration of the 1 year period.

Internal Review of Written Requests and Pediatric Studies. New section 505A requires the Secretary to establish an internal review committee to review all written requests. Members of the committee shall have expertise in pediatrics, biopharmacology, statistics, drugs and drug formulations, legal issues, pediatric ethics, the appropriate expertise pertaining to the pediatric product under review, one or more experts from the Office of Pediatric Therapeutics, and other individuals the Secretary designates.

New section 505A requires the Secretary to track and make available to the public the number of studies conducted, the specific drugs and biological products and their studied uses, types of studies conducted, number of pediatric formulations developed and not developed, labeling changes made due to the studies, annual summary of labeling changes made as a result of the studies conducted, and information regarding reports submitted on or after the date of enactment of the Act.

Relationship to Pediatric Research Requirements. New section 505A states that if a pediatric study is required by law or regulation other than BPCA, and it meets the completeness, timeliness, and other requirements of BPCA, it shall be deemed to satisfy the requirement for additional market exclusivity pursuant to BPCA.

Labeling Changes. New section 505A states that applications or supplements proposing a labeling change as a result of pediatric studies under BPCA shall be considered a priority application or supplement, and subject to the performance goals established by the Commissioner for priority drugs.

Within 180 days after the submission of the application, if the Commissioner determines that the sponsor and the Commissioner have been unable to reach agreement on appropriate changes to a drug label, then the Commissioner must request that the sponsor make any labeling change the Commissioner deems appropriate. If an application sponsor does not agree with the Commissioner's request for label change within 30 days, the matter is referred to the Pediatric Advisory Committee. The Committee shall consider the matter within 90 days and make recommendations to the Commissioner. The Commissioner then has 30 days to make a request to the sponsor of the application to make any labeling changes. If the sponsor still does not agree with the recommendations and fails to make a requested label change, the Commissioner may deem the drug misbranded.

Other Labeling Changes. New section 505A grants the Secretary the authority to order the label of a drug to include information

from studies demonstrating that a drug is or is not safe and effective in the pediatric population.

Dissemination of Pediatric Information. New section 505A requires the Secretary to make medical, statistical, and clinical pharmacology reviews of pediatric studies available to the public not later than 180 days after the date of submission of a report. The Secretary will also require the sponsors of studies that result in labeling changes to distribute this information to physicians and other healthcare providers.

Adverse Event Reporting. New section 505A requires the Secretary, during the one year period beginning on the date a labeling change is made, to ensure that all adverse event reports that have been received for a drug are referred to the Office of Pediatric Therapeutics established under BPCA and provided for review by the Pediatric Advisory Committee. The Pediatric Advisory Committee may choose to offer recommended actions in response to such reports to the Secretary.

Following the one year period, the Secretary must refer to the Office of Pediatric Therapeutics a report of all information regarding pediatric adverse events for a drug for which a pediatric study was conducted. When considering the report, the director of the Office of Pediatric Therapeutics may provide for the review of the report by the Pediatric Advisory Committee, including obtaining any committee recommendations regarding whether the Secretary should take action. The requirements of this subsection shall supplement, and not supplant, other reviews of such adverse event reports by the Secretary.

Clarification of Interaction of Market Exclusivity Under This Section and Market Exclusivity Awarded to an Applicant for Approval of a Drug Under 505(j). New section 505A states that if an abbreviated new drug application that is eligible for a 180 day period of market exclusivity under 505(j), and any or all of that period overlaps with the pediatric exclusivity period under this section, then the 180-day period shall be extended by the number of days of the overlapping period.

The granting of exclusivity under section 505A should not limit exclusivity under section 527, relating to orphan drugs, of this Act.

Referral if Pediatric Studies are not Completed. New section 505A states that if pediatric studies have not been completed and if the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population the Secretary shall: 1) for on-patent drugs, make a determination regarding whether an assessment shall be required to be submitted under the Pediatric Research Equity Act; and 2) for drugs that have no listed patents or have listed patents that have expired, determine whether there are Prescription Drug User Fee Act funds available to fund the requested studies. If the funds are not available, the Commissioner shall refer the drug for inclusion on the list established under section 409I of the Public Health Service Act for the conduct of studies.

New section 505A requires the Secretary to provide public notice of the decision not to require an assessment under section 505B and the basis of the decisions, name of any drug, its manufacturer, the indications to be studied pursuant to a grant made, and any

decision to refer a drug for inclusion on the list established under 409I of the Public Health Service Act.

Prompt Approval of Drugs Under Section 505(j) When Pediatric Information is Added to Labeling. New section 505A states that an abbreviated new drug application shall be not be considered ineligible for approval under 505(j) or misbranded under section 502 on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity. The Secretary may require that the labeling of a drug approved under section 505(j) include a statement that, because of marketing exclusivity for a manufacturer, the drug is not labeled for pediatric use and must include any appropriate pediatric contraindications, warnings, or precautions the Secretary deems necessary. This subsection does not affect the availability or scope of exclusivity.

Institute of Medicine Study. New section 505A requires the Secretary to request an IOM study of the written requests made and the studies conducted under BPCA, and report to Congress within three years of enactment of BPCA of 2007.

Sunset. New section 505A states that the authority to award exclusivity takes effect on the date of enactment and sunsets on October 1, 2012.

Section 502 amends section 409I of the Public Health Service Act to read as follows:

"Section 409I. Program for Pediatric Studies of Drugs."

List of Priority Issues in Pediatric Therapeutics. New section 409I requires the Secretary in conjunction with the Director of NIH, the FDA Commissioner, and experts in pediatric research to provide a list of priority issues in pediatric therapeutics that need studies (including drugs) within one year of enacting BPCA of 2007. The list shall be revised every three years, and will consider therapeutic gaps, specific pediatric diseases, and the adequacy of the pediatric research infrastructure.

Pediatric Studies and Research. New section 409I authorizes the Secretary, through NIH, to award funds to entities that have the expertise to conduct pediatric clinical trials or other research to enable the entities to conduct the drug studies or other research on the issues described via contracts, grants, or other appropriate funding mechanisms.

Process for Proposed Pediatric Study Requests and Labeling Changes. New section 409I allows the NIH Director to submit proposed pediatric study requests for consideration by the FDA Commissioner. The FDA Commissioner, in consultation with the NIH Director, may issue a written request based on a proposed pediatric study request from NIH to all holders of an approved application for the drug. If the FDA Commissioner does not receive a response to this written request, the Secretary shall publish a request for proposals to conduct the pediatric studies.

Once the award is granted and the study is completed, a report concerning the study shall be submitted to the NIH Director and the FDA Commissioner. The report will be made public and open for public comment. The FDA Commissioner then has 180 days to review the report and negotiate any labeling changes with the

holders of the approved applications. The Commissioner shall place the report and labeling change requests in the Federal Register.

New section 409I outlines a dispute resolution process if label changes are not made within 180 days of submission of the application. If an application sponsor does not agree with the Commissioner's request for label change within 30 days, the matter is referred to the Pediatric Advisory Committee. The Committee shall consider the matter within 90 days and make recommendations to the Commissioner. The Commissioner then has 30 days to make a request to the sponsor of the application to make any labeling changes. If the sponsor still does not agree with the recommendations, the Commissioner may deem the drug misbranded.

Dissemination of Pediatric Information. New section 409I requires the Secretary, through NIH, within a year of passage, to conduct a study on the feasibility of establishing a compilation of information on pediatric drug use and to report the findings to Congress.

Authorization of Appropriations. New section 409I authorizes $200 million in FY2008 and such sums as necessary for the following 4 fiscal years to conduct pediatric studies. PDUFA is amended to include activities relating to the support of off-patent studies of drugs on pediatric populations.

Continuation of Operation of Committee. New section 409I allows the pediatric subcommittee of the Oncologic Drugs Advisory Committee to continue to operate for five years beginning on the date of enactment of BPCA 2007.

Pediatric Subcommittee of the Oncologic Drugs Advisory Committee. New section 409I allows the pediatric subcommittee of the Oncologic Drugs Advisory Committee to continue to operate for five years beginning on the date of enactment of BPCA 2007. This committee is allowed to provide recommendations to the internal review committee on the implementation of PREA and BPCA with respect to treating pediatric cancers.

Effective Date and Limitation for Rule Relating to Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products. New section 409I mandates the proposed FDA rule entitled "Toll-Free Number for Reporting Adverse Events on Labeling for Human Drug Products" to take effect on January 1, 2008, unless the Commissioner issues the final rule earlier.

TITLE VI. REAGAN-UDALL FOUNDATION FOR THE FOOD AND DRUG ADMINISTRATION

Section 601. The Reagan-Udall Foundation for the Food and Drug Administration

Chapter VII of the Federal Food, Drug, and Cosmetic Act is amended by adding at the end the following:

> "Subchapter I—Reagan-Udall Foundation for the Food and Drug Administration"
>
> *"Section 770. Establishment and Functions of the Foundation."*

In General. New section 770 provides for the establishment of a non-profit corporation, independent of the U.S. Government, to be

known as the Reagan-Udall Foundation for the Food and Drug Administration.

Purpose of Foundation. New section 770 states the purpose of the Foundation is to advance the mission of FDA to "modernize medical, veterinary, food, food ingredient, and cosmetic product development, accelerate innovation, and enhance product safety."

Duties of the Foundation. New section 770 states that the Foundation shall advance the Critical Path Initiative to identify unmet needs in the sciences of developing, manufacturing, and evaluating the safety and effectiveness of diagnostics, devices, biologics, and drugs; establish goals and priorities to meet such unmet needs; assess Federal intramural and extramural research and development programs, and facilitate interagency coordination of such programs; release, publish, license, and distribute material, reagents, and techniques to meet such goals and priorities; take the necessary actions to patent and license inventions developed through the Institute; and provide objective clinical and scientific information to FDA and other Federal agencies.

Board of Directors. New section 770 states the Foundation shall have a Board of Directors composed of both appointed and ex-officio members. Ex-officio members of the Board include the Commissioner of Food and Drugs, the Director of NIH, the Director of the Centers for Disease Control and Prevention, and the Director of AHRQ. The ex-officio members shall appoint 12 Board members as outlined in the bill.

New section 770 requires the Secretary to convene a meeting of the ex-officio members of the Board within 30 days of enactment of this Act to incorporate the Foundation and appoint the members of the Board and its Chair. The terms of service of the ex-officio members shall then terminate.

New section 770 states that the Board shall establish by-laws and polices for the selection of officers, employees, agents, and contractors of the Foundation; acceptance of donations; conflicts of interest; licensure and publication; review of proposals and awarding of grants; specification of a cap for administrative expenses; execution of memoranda of understanding; funding of training fellowships; annual Board review; and duties of the Executive Director. The Board shall also prioritize and provide overall direction to the activities of the Foundation, evaluate the performance of the Executive Director, and carry out any other necessary activities regarding the functioning of the Foundation.

Members of the Board shall serve a four-year term and may not receive compensation for service on the Board.

Incorporation. New section 770 requires the ex-officio members of the Board to serve as incorporators.

Nonprofit Status. New section 770 states that the Foundation shall be considered a non-profit corporation.

Executive Director. New section 770 states that an Executive Director shall be appointed by the Board and shall be responsible for the day-to-day operations of the Foundation. The compensation of the Executive Director shall not exceed the compensation of the Commissioner.

Administrative Powers. New section 770 states that the Executive Director may use a corporate seal; hire, promote, and discharge officers and employees; oversee personal property, general

operations, and privileges granted to the Board of the Foundation; enter into and modify contracts; oversee financials; and exercise other powers granted.

Acceptance of Funds from Other Sources. New section 770 allows the Executive Director to solicit and accept any funds and property on behalf of the Foundation to carry out the duties of the Foundation.

Service of Federal Employees. New section 770 allows Federal employees to serve on advisory committees to the Foundation and "otherwise cooperate with and assist the Foundation" or be detailed to the Foundation.

Detail of Government Employees. New section 770 allows Federal Government employees to be detailed from Federal agencies to the Foundation with or without reimbursement to those agencies at any time.

Annual Reports. New section 770 requires any recipient of a grant, contract, fellowship, memorandum of understanding, or cooperative agreement from the Foundation to provide annual reports on their activities. The Executive Director shall provide annual reports to FDA and to Congress describing the activities of the Foundation, recommendations for incorporating outcomes into FDA "regulatory and product review activities," and financial accounting of its funds beginning with FY 2009.

Separation of Funds. New section 770 requires funds received from the Treasury to be held in separate accounts from funds received from private entities.

Funding. New section 770 prohibits the FDA Commissioner from transferring less than $500,000 and no more than $1,250,000 to the Foundation from FDA appropriated funds.

Section 601 further amends Chapter VII of the Federal Food, Drug, and Cosmetic Act by adding at the end the following:

"Section 771. Location of Foundation."

New section 771 requires the Foundation to be located "not more than 20 miles from the District of Columbia."

"Section 772. Activities of the Food and Drug Administration."

In General. New section 772 requires the Commissioner to receive and assess the report submitted to the Commissioner by the Executive Director of the Foundation.

Report to Congress. New section 772 requires the Commissioner, beginning with FY2009, to submit an annual report to Congress summarizing the Executive Director's report to FDA and Congress.

Extramural Grants. New section 772 states this subchapter shall have no effect on any grant, contract, memorandum of understanding, or cooperative agreement between the Food and Drug Administration and any other entity entered into before, on, or after the date of enactment of this Act.

Section 602. Office of the Chief Scientist

Section 602 amends chapter IX of the Federal Food, Drug, and Cosmetic Act by adding at the end the following:

"Section 910. Office of the Chief Scientist."

Establishment; Appointment. New section 910 states the Secretary shall establish an office of the Chief Scientist within the Office of the Commissioner, and shall appoint a Chief Scientist to lead the office.

Duties of the Office. New section 910 states the Office of the Chief Scientist shall oversee and coordinate intramural research of FDA; track intramural research awards made by the Food and Drug Administration to avoid research duplication; develop and advocate for a budget for intramural research; develop a peer-review evaluation process for intramural research; and identify and solicit research proposals from across FDA through an advisory board.

Section 603. Critical path public-private partnerships

Section 603 amends subchapter E of chapter V of the Federal Food, Drug, and Cosmetic Act by adding at the end the following:

"Section 566. Critical Path Public-Private Partnerships."

Establishment. New section 566 states that the Secretary, acting through the Commissioner, shall enter into collaborative agreements to implement the Critical Path Initiative of FDA. This shall be done by developing innovative, collaborative projects in research, education, and outreach for the purpose of fostering medical product innovation, enabling the acceleration of medical product development, and enhancing medical product safety.

Eligible Entity. New section 566 outlines criteria to be considered an 'eligible entity.'

Funding. New section 566 states eligible entities may not accept funding for a Critical Path Public-Private Partnership project from any organization that manufactures or distributes products regulated by FDA unless funding comes from two or more of such organizations and the entity assures FDA that the results of the Partnership will not be influenced by any source of funding.

Annual Report. New section 566 requires the Secretary, beginning not later than 18 months after enactment of this section, to submit annual reports to Congress reviewing the operations and activities of the Partnerships in the previous year.

Definition. New section 566 defines the term 'medical product' to include drugs, biological products, devices, or combinations of these products.

Authorization of Appropriations. New section 566 authorizes $5,000,000 for fiscal year 2008 and such sums as may be necessary for each of fiscal years 2009 through 2012 to carry out this section.

TITLE VII—CONFLICTS OF INTEREST

Section 701. Conflicts of interest

Section 701 amends subchapter A of chapter VII of the Federal Food, Drug, and Cosmetic Act by inserting at the end the following:

"Section 712. Conflicts of Interest."

Definitions. New section 712 defines the terms "advisory committee" and "financial interest.

Appointments to Advisory Committees. New section 712 directs the Secretary to recruit advisory committee members through var-

ious offices of FDA and with direction from professional societies. The Secretary shall consider the advisory committees with the largest number of vacancies. The Secretary may advertise the process for becoming an advisory committee member, and set forth guidelines for such advertising. Recruitment may also take place through entities receiving funding from various Federal health agencies.

New section 712 requires the Secretary, in appointing advisory committee members, to take into account the expertise of the individual, as well as the financial disclosure report the candidate has filed, so as to reduce the likelihood that the individual will require written waivers when serving on the advisory committee.

Individuals with financial interest in a matter before an advisory committee may, at the discretion of the Secretary, be allowed to participate in an advisory committee meeting as a guest expert, but may not participate in the committee's discussion or voting.

Granting and Disclosure of Waivers. New section 712 requires each member of an advisory committee to disclose to the Secretary all relevant financial interests before an advisory committee meeting. An advisory committee member shall be prohibited from voting with respect to any matter considered by the committee if the member (or immediate family member of such member) has a financial interest that could affect the member's decision.

New section 712 allows the Secretary to grant a waiver if necessary to afford the committee the benefit of the member's expertise. The Secretary may not grant more than one waiver per committee member, and no waiver may be granted if the member's own scientific work is under review. The Secretary must disclose on the FDA website, 15 or more days in advance of the advisory committee meeting, any waivers, determinations, or certifications the Secretary has granted, the reasons for such waivers, determinations, or certifications, and the type, nature, and magnitude of the financial interests of the committee member to which the waiver, determination, or certification applies.

Public Record. New section 712 requires the Secretary to ensure that the public record and transcript of each meeting of an advisory committee includes the disclosure of waivers, determinations, or certifications pertaining to that meeting.

Annual Report. New section 712 requires the Secretary to submit to various congressional committees an annual report on advisory committee vacancies and the number of disclosures required by this act.

Periodic Review of Guidance. New section 712 states that the Secretary shall review FDA guidance documents on conflicts of interest waiver determinations with respect to advisory committees at least once every five years.

Additionally, the Committee strongly encourages FDA to reconsider its decision to terminate the Medical Imaging Drugs Advisory Committee (MIDAC). Accordingly, the Committee directs FDA to either re-establish this advisory committee, or provide a detailed explanation of why it is not re-establishing this advisory committee. This should be done not later than six months after enactment of this act.

TITLE VIII—CLINICAL TRIAL DATABASES

Section 801. Clinical trial registry database and clinical trial results database

Section 801 amends title IV of the Public Health Service Act by striking subsection (i) of section 402 and inserting the following after section 492B:

"Section 492C. Clinical Trial Registry Database; Clinical Trial Results Database."

Definitions. New section 492C defines the terms applicable clinical trial, clinical trial information, completion date, device, drug, and responsible party. Current law requires the registration of certain drug trials; this section extends its requirements to certain trials conducted on drugs, devices, and biologics. Current law generally pertains to clinical trials testing treatments of serious or life-threatening diseases or conditions. This section expands this aspect as well, as it generally pertains to phase II—IV studies—(whether Federally or privately funded, and whether on an approved or unapproved product)—that test a product's safety or effectiveness. This section's requirements would also apply to trials conducted outside of the United States on products with or seeking FDA approval. Current law specifies that required clinical trial information is to be forwarded to the data bank by the sponsor of the trial. This section requires action by the trial sponsor, or alternately, in certain circumstances, by the principal investigator.

The definition of completion date deems a trial complete after the final collection of data from subjects for the primary and secondary outcomes to be examined in the trial. The default responsible party (RP) is the trial sponsor. This section enables the principle investigator to act as the RP, only if he or she was responsible for conducting the trial, had access to and control over the data, had the right to publish results of the trial, and had the responsibility to meet all of the bill's requirements.

Clinical Trials Registry Database. New section 492C categorizes clinical trials registry database provisions into those addressing registry establishment, contents format, data submission, truthful clinical information, timing of submission, and updates.

Establishment. New section 492C requires the Secretary of Health and Human Services, acting through the Director of the National Institutes of Health (Director), to establish and maintain a clinical trials registry. The information in the registry shall be made public via a Web site on the Internet.

Contents. New section 492C significantly expands the contents of the registry. Current law specifies that the registry should contain eligibility criteria, trial locations, an enrollment point of contact, and a description of whether and how requests for single-patient and expanded protocol use of the new drug would be addressed. The requirements are expanded to include the elements of the World Health Organization's (WHO's) International Clinical Trials Registry Platform registration data set: city, State, and zip code for each trial location; estimated completion date; RP contact information; restrictions on non-RP employee's ability to discuss or publish trial results; and other data, as appropriate.

Format and Structure. New section 492C requires that database entries be easily compared, and that the registry be searchable by indication being studied, safety issue, enrollment status, and sponsor.

Data Submission and Truthful Clinical Information. New section 492C requires the RP to submit required registry information to the Director, and the information may not be false or misleading. The clinical trial information will not be required to include information from any source other than the trial.

Timing of Submission and Updates. New section 492C states the timing of submission will be linked to patient enrollment (within 14 days). Notice of trial completion and changes in enrollment status must be submitted within 30 days of the respective events. Updates, reflecting the dates of any changes, must be submitted once every six months until information on the results of the trial are submitted to the results database.

Clinical Trials Results Database. New section 492C requires the Secretary, acting through the Director, to establish and administer a clinical trial results database, made publicly available via the Internet. Details of the results publication requirements are presented below.

Searchable Categories. New section 492C requires the Director to ensure that the database is searchable by the indication being studied, safety issue, FDA application status, trial phase, product name, and the trial's primary sponsor and other financial sponsors.

Contents. New section 492C requires the RP to submit to the Director for inclusion in the results database two summaries and several pieces of information. One summary will be in non-technical language understandable to patients, and will include the trial purpose, sponsor, point of contact for information about the clinical trial, patient population, and a general description of the clinical trial results including changes in trial design and any significant safety information. The second summary will be technical, and will include the same elements as the non-technical summary as well as each financial sponsor (not just the primary sponsor), and a summary of results describing primary and secondary endpoints, as well as significant safety information. The additional pieces of information will include information regarding any subjects who ceased participation in the trial, agreements that would prevent non-employees of the RP from discussing or publishing trial results, links to peer-reviewed publications of trial results, trial completion date, and links to any relevant FDA adverse regulatory actions.

Timing. New section 492C requires, in general, the RP to submit information to the Director within one year after the earlier of the actual or estimated trial completion date, or trial termination date. The Director could grant one or more extensions for good cause. The RP will be required to submit biannual updates reflecting changes in previously submitted data for a decade following the initial submission, except that changes in FDA regulatory status would be required to be submitted within 30 days after the change.

Truthful Clinical Trial Information. New section 492C states, as was the case for the registry, for the results database, information submitted by an RP may not be false or misleading, and informa-

tion will not be required from any source other than the clinical trial involved.

Public Availability of Results. New section 492C requires the Director to make results information publicly available at different times, depending on the type of information. For pre-approval studies, the publication date will occur within a certain period following either: (1) FDA product approval or clearance, or (2) FDA issuance of a not approvable or not substantially equivalent letter. Trial results will be required to be made public within 30 days of such actions, and FDA medical and clinical pharmacology reviews of the pre-approval studies will be made public within 90 days.

For post-approval studies, results will be required to be made public within 30 days of submission, unless the RP certified that he or she filed, or will file within one year, an FDA application for a new use of the product. In that case, the results will be required to be made public within 30 days after: (1) FDA new use approval or clearance, (2) FDA issuance of a not approvable or not substantially equivalent letter, (3) withdrawal of the application, or (4) two years following the certification. FDA medical and clinical pharmacology reviews will be required to be made public within 90 days of requirements 1 through 3.

The date trial results are required to be made public in the results database could be postponed for up to two years if the RP is seeking publication in a peer-reviewed journal. In this case, clinical trial information will not be required to be made public under the Freedom of Information Act (5 U.S.C. 522; FOIA). In a period during which the Director has received, but not made public clinical trial information in accordance with the provisions of the bill, the Director will be required to respond to requests from other Federal agencies and peer-reviewed journals that clinical trial information has been submitted, but has not yet been made public.

Updates; Tracking of Changes in Submitted Information. New section 492 requires the Director to ensure that updates made by the RP to the registry and results database do not result in the removal of original submissions or previous updates, and that the public shall have access to previous submissions and be able to track changes.

Coordination and Compliance. The Secretary will be required to consult with heads of other agencies that conduct human studies to determine if such studies are applicable clinical trials and to develop with such agencies appropriate procedures to ensure that clinical trial information for such applicable trials is submitted to the registry and databases established under this title.

New section 492C requires the Director to link corresponding entries in the registry and results database. If the Director locates a missing results database entry, the RP will be given notice and an opportunity for correction. If the correction is not made, the Director will report the noncompliance to the relevant Federal agency's scientific peer review committee and to the Office of Human Research Protections, and post notice of the failure in the registry.

New section 492C requires the Secretary, acting through the FDA Commissioner, to verify that required clinical trial information has been submitted when considering a product application. After notice to the RP and an opportunity to correct noncompliance,

the Secretary will be required to refuse to file, approve, or clear the application or premarket notification.

New section 492C requires the Secretary to take certain steps to ensure that results database summary documents are not false or misleading, and to give RPs notice and an opportunity to correct noncompliance.

Penalties for Noncompliance. New section 492C states it shall be unlawful to fail to submit required clinical information, or to submit false, or misleading information. The Secretary could, after considering specific factors, such as whether the RP had engaged in a pattern of noncompliance, apply penalties. In addition to the penalties under §303(a) of the FFDCA, this bill includes additional new penalties including a fine of not more than a total of $15,000 for all violations adjudicated in a single proceeding in the case of an individual, and not more than $10,000 per day until the violation is corrected in the case of any other person. If the case, however, is against an individual or a non-profit entity, the penalty may not exceed $15,000 for all violations adjudicated in a single proceeding.

Authorization of Appropriations. New section 492C authorizes $10 million to be appropriated for any fiscal year.

Conforming Amendments. New section 492C includes conforming provisions that amend relevant sections of the FFDCA and Public Health Service Act.

Guidance. New section 492C requires the FDA Commissioner, in consultation with the Director of the National Institutes of Health, to issue guidance to clarify which clinical trials are required to be submitted for inclusion in the registry.

Preemption. New section 492C provides that States are prohibited from requiring the registration of clinical trials or the posting of their results. Submissions that are in compliance with new section 492C are prohibited from being considered either (1) by the Secretary as evidence of a new intended use different from labeling, or (2) as labeling, adulteration, or misbranding under the FFDCA.

Effective Dates. New section 492C requires the Secretary to establish the registry and results database within one year of the Act's date of enactment. Trials initiated after the date of enactment and before the date the registry is established will have 120 days from establishment to submit information. Trials completed after the Act's date of enactment and before the results database is established will have 180 days after establishment to submit information, except that such trials involving a drug to treat a serious or life-threatening condition will have 90 days after establishment to submit results.

New section 492C states that information about trials initiated or concluded before the date of enactment may be voluntarily submitted to the registry or results database. The Secretary may require such information to be submitted if it is in the interest of public health.

New section 492C states that the Secretary shall consult with other agencies to determine if their human studies are applicable clinical trials and to develop procedures to ensure that clinical trial data is submitted 210 days after the date that the registry and results database were established. After receiving public comment

and within 90 days of enactment, the Secretary will be required to publish a notice determining whether to build upon or supplant the current Federal registry (clinicaltrials.gov). If supplanted, the current registry will be required to be maintained as an archive.

Section 802. Study by Government Accountability Office

Section 802 states, not later than one year after enactment of this section, the Comptroller General of the United States shall report to Congress on whether information on the trials registry and database is considered promotional and to evaluate the implementation of this database.

TITLE IX—RISK EVALUATION AND MITIGATION STRATEGIES

Section 901. Postmarket studies and clinical trials regarding human drugs; risk evaluation and mitigation strategies

Section 901 amends section 505 of the Federal Food, Drug, and Cosmetic Act by adding at the end the following subsections:

"(o). Postmarket Studies and Clinical Trials; Labeling."

In General. New subsection (o) states that a responsible person may not introduce or deliver into interstate commerce the new drug involved if the person is in violation of postmarket studies or clinical trials required by the Secretary or by safety labeling changes requested by the Secretary.

Definitions. New subsection (o) defines the terms responsible person, and covered application.

Studies and Clinical Trials. New subsection (o) states that the Secretary may require a responsible person (a product sponsor) to conduct a post-approval study of the drug, or a post-approval clinical trial of the drug, on the basis of scientific information, including information regarding chemically-related or pharmacologically-related drugs. The purpose of such study or trial is to assess a known serious risk related to the use of the drug involved, assess signals of a serious risk related to the use of the drug, or to identify a serious risk.

New subsection (o) states after approval of a covered application, the Secretary may require a post-approval study or trial only if the Secretary becomes aware of new safety information. For such a study, the applicant must submit a timetable for completion of the study and shall periodically report on the status of the study to the Secretary.

The applicant shall be deemed in violation of this subsection unless the applicant demonstrates good cause for failure to comply with such a timeline. Good cause is to be defined by the Secretary.

The Committee expresses its concern with the historical underrepresentation of medically underserved populations in clinical trials and post-market drug research. The Committee urges FDA to identify and retain an employee who will study and report on ways in which to increase diversity in clinical trials and post-market drug research. The individual should consider how studies of drugs, medical devices, vaccines, and other medical devices regulated by the FDA should include the collection, statistical analysis and interpretation of data on medically underserved populations. The Committee urges the FDA to encourage diverse populations to par-

ticipate in clinical trials and post-market drug research. Furthermore, the FDA should provide a report to Congress annually on the FDA's progress in increasing diversity in clinical trials and post-market drug research.

Safety Labeling Changes Requested by Secretary. New subsection (o) requires the Secretary to promptly notify the responsible person should the Secretary become aware of new safety information that the Secretary believes should be included in the labeling of the drug.

New subsection (o) requires the responsible person, within 30 days of notification, to either submit a supplement proposing changes to the approved labeling to reflect the new safety information or notify the Secretary that the responsible person does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

Upon receipt of such supplement, the Secretary will review the supplement. If the Secretary disagrees with the proposed changes by the responsible person, the Secretary shall initiate discussions with the responsible person to reach agreement on whether the labeling changes for the drug should be modified to reflect the new safety information and, if so, the contents of such labeling changes. Discussions will not last more than 30 days after the response to the notification unless the Secretary determines an extension is necessary. Within 15 days of the conclusion of the discussions, the Secretary may issue an order directing the responsible person to make such a labeling change as the Secretary deems appropriate to address the new safety information. Within 15 days of such an order, the responsible person shall submit a supplement containing the labeling change.

New subsection (o) allows the responsible person, within five days of receiving an order, to appeal using the Food and Drug Administration's normal dispute resolution procedures established by the Secretary in regulation and guidance.

If the required label change is not made by the date specified, the responsible person shall be deemed in violation of this section.

If the Secretary concludes that a labeling change is necessary to protect against a serious public health threat, the Secretary may accelerate the timelines set forth above.

"(p). Risk Evaluation and Mitigation Strategy (REMS)."

In General. New subsection (p) states a person may not introduce or deliver for introduction into interstate commerce a new drug if a risk evaluation and mitigation strategy is required with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy, or a postmarket strategy is required and the Secretary, after notice and opportunity for a hearing, publishes in the Federal Register a statement that the person is not cooperating with the Secretary in developing such a strategy for the drug.

The Secretary may not approve an application for a new drug or biological product or supplement unless the product sponsor has submitted to the Secretary a statement that states whether a REMS strategy or a postmarket study or clinical trial is necessary. The statement must take into account the following five factors: size of the population likely to use the drug involved; seriousness

of the disease or condition that the drug shall treat; expected benefit of the drug with respect to such disease or condition; expected or actual duration of treatment with the drug; and the seriousness of any known or potential adverse events that may be related to the drug.

Section 901 amends chapter V of the Federal Food, Drug, and Cosmetic Act by inserting after section 505 the following section:

"Section 505–1. Risk Evaluation and Mitigation Strategies."

Submission of Proposed Strategy. New section 505–1 states for new drug and biologic license applications, if the Secretary determines a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug involved outweigh the risks of the drug, a person must submit, as part of the application, a proposed risk evaluation and mitigation strategy. The Secretary must consider the statement along with the following factors:

a. The estimated size of the population likely to use the drug involved;

b. The seriousness of the disease or condition that is to be treated;

c. The expected benefit of the drug with respect to such disease or condition;

d. The expected or actual treatment with the drug;

e. The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug;

f. The availability and safety of a drug or other treatment, if any, for such disease or condition to which the safety of the drug may be compared; and

g. Whether the drug is a new molecular entity;

New section 505–1 states that for those drugs or biologics that have been approved, the Secretary may subsequently require a risk evaluation and mitigation strategy if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug. Within 120 days after the Secretary notifies the holder of an approved covered application, the holder must submit to the Secretary a proposed risk evaluation and mitigation strategy. The authority of the Secretary to require a risk evaluation and mitigation strategy also applies to supplemental applications seeking approval of a new indication for use of the drug. Abbreviated new drug applications may also be subject to REMS requirements for medication guides or patient package inserts and restrictions on distribution or use.

Definitions. New section 505–1 defines adverse drug experience, covered application, new safety information, serious adverse drug experience, serious risk, signal of a serious risk, responsible person, and unexpected serious risk.

Contents. New section 505–1 requires a proposed risk evaluation and mitigation strategy to include a timetable and may include additional elements, including medication guides or patient package inserts, communication plans, and restrictions on distribution or use.

Minimal Strategy. New section 505–1 requires that a risk evaluation and mitigation strategy be assessed at least once annually

for the first three years after the strategy is initially approved, an assessment in the seventh year after approval of the REMS, and for subsequent years, assessments are increased or reduced in frequency as necessary. After the initial three year period, the Secretary may eliminate a REMS if the Secretary determines that the serious risks of the drug have been adequately identified and assessed and are adequately being managed.

Additional Potential Elements of Strategy. The Secretary may require that the REMS for a drug include one or more of the additional elements listed in the bill. These include medication guides or patient package inserts, and a communication plan to health care providers, if the Secretary determines such plan may support implementation of the strategy.

The Committee is aware that pharmacies may not be able to obtain Medication Guides in an efficient manner so that they can be distributed to patients with their prescriptions. The Committee is also aware that FDA held a public meeting in June to solicit input from stakeholders on how the agency might address some of the implementation issues in the Medication Guide program. We urge that the agency take expeditious action in making changes to the program so that the program is more effective in providing patients with Medication Guide information and pharmacies can provide these important information sheets to patients. Among the changes we urge FDA to make as soon as possible relate to the ability of pharmacies to print these Medication Guides electronically as part of the "single pass" information that they print as part of filling the prescription (i.e., labels, receipts, warning labels, etc.) The Committee believes that the electronic printing of Medication Guides by pharmacies through this method would increase the distribution of Medication Guides. The Committee urges that FDA work with pharmacies and information vendors to assure that Medication Guides are properly formatted for electronic distribution and are electronically printed in such a way that the ability of patients to read and understand the information in the Medication Guide is not compromised. This may include FDA issuing guidance on electronic distribution and printing of Medication Guides. The Committee also urges that FDA explore the option of allowing pharmacies to distribute these Medication Guides to patients (upon request) through electronic mail.

Additionally, the Committee is also concerned that pharmacies are having difficulty in obtaining these Medication Guides because of the number of such leaflets that are now required to be distributed. The Committee asks that FDA report to the Committee on specific steps that are being taken to streamline the process by which these Medication Guides are obtained by pharmacies and distributed by manufacturers. This would include evaluating the feasibility of a single access point for pharmacies in obtaining these Medication Guides.

The Committee urges the FDA Commissioner to expand the functions of the Risk Communication Advisory Committee to advise that the dissemination and communication of the risks and benefits of drugs, biologics, and devices to health disparity populations, individuals with disabilities or cognitive impairments, and senior citizens be done in a manner and formats that are appropriate and accessible and which take into account relevant factors that limit ac-

cess to information, including language barriers; to healthcare providers, accounting for the diversity among providers in terms of practice, affinity for technology, and focus; and advising on the dissemination of risk and benefit information through multiple media platforms.

Restrictions on Distribution or Use. If the Secretary determines that a drug shown to be effective can be safely used only if distribution or use of such drug is restricted, the Secretary may require, as elements of the risk evaluation and mitigation strategy, such restrictions on distribution or use as are needed to ensure safe use of the drug. Such restrictions on distribution or use must be commensurate with a specific serious risk listed in the labeling of the drug, not be unduly burdensome on patient access to the drug, and, to the extent practicable, minimize the burden on the healthcare delivery system. Within 30 days of requiring a restriction on distribution or use, the Secretary must publicly post an explanation of how such elements will mitigate the observed safety risk.

New section 505–1 states that restrictions on distribution or use may require one or more of the following: healthcare providers that prescribe the drug have special training or experience; pharmacies, practitioners, or healthcare settings that dispense the drug are specially certified; the drug be dispensed to patients only in certain healthcare settings; the drug be dispensed to patients with evidence or other documentation of safe-use conditions; each patient using the drug be subject to certain monitoring; or each patient using the drug be enrolled in a registry.

New section 505–1 states that the restrictions on distribution of use may require a system through which the responsible person is able to monitor and evaluate the implementation of the restrictions; work to improve implementation of the restrictions by parties in the healthcare system who are responsible for implementing the restrictions; and notify those drug wholesalers who have failed to meet their responsibilities for implementing the restrictions.

New section 505–1 requires the holder of an approved application that is subject to distribution restrictions under this subsection to provide the sponsor seeking approval of an abbreviated new drug application a sufficient quantity of the drug to conduct bioequivalence testing if the sponsor meets two requirements. First, the sponsor must agree to such restrictions on distribution as the Secretary finds necessary to assure safe use of the drug during bioequivalence testing. When the sponsor seeking the abbreviated new drug application has agreed to the restrictions necessary to assure safe use of the drug during bioequivalence testing, the Secretary shall issue to the sponsor a letter that describes the Secretary's finding and serves as proof that the sponsor has satisfied the requirements. Next, the sponsor must pay the holder of the approved application the fair market value of the drug purchased for bioequivalence testing.

New section 505–1 requires the Secretary, acting through the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration, to seek input from patients, physicians, pharmacists, and other healthcare providers about how elements to assure safe use of one or more drugs may be standardized so as not to be unduly burdensome on patient access to the drug

and minimize the burden on the healthcare delivery system. At least once a year, the Drug Safety and Risk Management Advisory Committee shall evaluate for one or more drugs the elements to assure safe use. Considering such input and evaluations, the Secretary shall issue or modify agency guidance about how to implement the requirements and may modify elements under this subsection for one or more drugs where appropriate.

New section 505–1 allows the Secretary, in public health emergencies, to waive any restriction on distribution or use.

Assessment and Modification of Approved Strategy. New section 505–1 states that, for voluntary assessments, the responsible person involved may submit to the Secretary an assessment of, and proposed modification to, the approved strategy for the drug at any time.

For required assessments, a responsible person must submit an assessment of, and may propose a modification to, the approved risk evaluation and mitigation strategy for a drug under one of four situations:

1. when submitting a supplemental application for a new indication for use;
2. when required by the strategy;
3. within a time period to be determined by the Secretary, if the Secretary determines that new safety or effectiveness information indicates that either a timetable, medication guide, or communication plan should be modified or included in the strategy, or an element regarding restricted distribution or use should be modified or included in the strategy; or
4. within 15 days when ordered by the Secretary, if the Secretary determines that there may be a cause of for action by the Secretary under section 505(e).

Label changes that do not require submission to the Secretary or for which distribution of the drug involved may commence upon the receipt by the Secretary of a supplemental application for the change do not require a REMS assessment.

Review of Proposed Strategies; Review of Assessments of Approved Strategies. New section 505–1, in general, requires the Secretary to promptly review each proposed risk evaluation and mitigation strategy for a submitted drug and promptly review each assessment of an approved risk evaluation and mitigation strategy.

New section 505–1 states the Secretary may require the applicant to submit information regarding its marketing plan and practices for the drug, so as to allow the Secretary to determine whether any of the proposed or ongoing marketing activities undermine any of the requirements of the risk evaluation and mitigation strategy.

New section 505–1 states that unless the responsible person requests the dispute resolution process, the Secretary must approve and describe the REMS for a drug, or any modification to the strategy, as part of the action letter on the application or in an order issued within 50 days after the date discussions of such modification begin. An approved REMS shall remain in effect until the Secretary acts. Any action letter or order shall be made publicly available.

New section 505–1 states not earlier than 15 days, and not later than 35 days, a responsible person may request in writing that a

dispute about the strategy be reviewed by the Drug Safety Oversight Board. The Board may look at the elements of the REMS, but may not determine whether a REMS is necessary.

New section 505–1 allows the Secretary to convene a meeting of one or more advisory committees of the Food and Drug Administration to review a concern about the safety of a drug or class of drugs; review the REM strategy or strategies of a drug or group of drugs; or to review a dispute between the Secretary and a responsible person.

When a concern about a serious risk of a drug may be related to the pharmacological class of the drug, the Secretary may defer assessments of the approved REMS for such drugs until the Secretary has convened one or more public meetings to consider possible responses to such concern. If the Secretary defers such an assessment, the Secretary must give public notice of such action within five days. After considering the discussions from any public meeting under this subparagraph, the Secretary may announce in the Federal Register a planned regulatory action, seek public comment about such action, and, after seeking such comment, issue an order addressing such regulatory action.

Abbreviated New Drug Applications. New section 505–1 states, in general, a drug that is the subject of an abbreviated new drug application under section 505(j) is subject only to two elements of a REMS strategy if the listed drug is subject to a REMS that also contains those elements. The two elements are a medication guide or patient package insert and restrictions on distribution or use. A listed drug and its abbreviated new drug application shall use a single, shared system with regard to restrictions in distribution or use. The Secretary, however, may waive such a requirement if the Secretary determines that it is either not practical or the burden of using the single, shared system outweighs the benefit of not using this system.

New section 505–1, for an applicable listed drug for which a drug is approved under section 505(j), requires the Secretary to undertake any communication plan to healthcare providers and to inform the responsible person of any modification to the REMS of the applicable listed drug.

Drug Safety Oversight Board. New section 505–1 establishes a Drug Safety Oversight Board. The Board shall be composed of Federal employees who are scientists and healthcare providers; representatives from offices throughout the Food and Drug Administration, include at least one representative from each of the National Institutes of Health and the Department of Health and Human Services, and other representatives from appropriate Federal agencies the Secretary designates. The Board will meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.

Section 901 amends section 301 of the Federal Food, Drug, and Cosmetic Act by adding at the end the following:

"(jj) The dissemination of a television advertisement without complying with section 503B."; and by inserting after section 503A the following:

"Section 503B. Prereview of Television Advertisements."

New section 503B, in general, allows the Secretary to require the submission of any television advertisement for a drug (including any script, story board, rough, or a completed video production of the television advertisement) for review not later than 45 days before dissemination of the television advertisement.

New section 503B allows the Secretary, in conducting a review of a television advertisement, to make recommendations on changes that are necessary to protect the consumer or consistent with prescribing information for the product under review. If appropriate and if information exists, the Secretary may make recommendations on statements for inclusion in the advertisement to address the specific efficacy of the drug as it relates to a specific population group. The Secretary is not authorized to make or direct changes in any submitted material.

New section 503B states in cases where the Secretary determines that the advertisement would be false or misleading without a specific disclosure about a serious risk listed in the labeling of the drug involved, the Secretary may require inclusion of such disclosure in the advertisement. The Secretary may require the advertisements to include, within the first two years from the date of the approval of the drug under section 505, a specific disclosure of such date of approval if the Secretary determines that the advertisement would otherwise be false or misleading.

Direct-to-Consumer Advertisements. New section 503B states, in general, in the case of an advertisement for a prescription drug presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear and conspicuous manner. The Secretary of Health and Human Services shall issue a regulation establishing standards for determining whether a major statement relating to side effects and contraindications of a drug is presented in a clear and conspicuous manner.

Civil Penalties. New section 503B states any person who disseminates a direct-to-consumer advertisement that is false or misleading shall be liable to the United States for a civil penalty in an amount not to exceed $250,000 for the first such violation in any 3-year period, and not to exceed $500,000 for each subsequent violation in any 3-year period. Prior to written notice by the Secretary of an order to assess a penalty, repeated dissemination of the same or similar advertisement shall be considered one violation. On and after the date of the receipt of a written notice, all violations that occur in a single day shall be considered one violation.

With respect to advertisements that appear in magazines or other publications that are published less frequently than daily, each issue date (e.g., week, month) should be treated as a single day for purposes of calculating the number of violations.

New section 503B allows the Secretary, after providing written notice to the person to be assessed a civil penalty and an opportunity for a hearing, to assess a civil penalty by an order made on the record. Upon request of the person to be assessed a civil penalty, the Secretary shall take into account the nature, circumstances, extent, and gravity of the violation or violations.

New section 503B states no person shall be required to pay a civil penalty if the person submitted the advertisement for review and after incorporating any comment received from the Secretary in the advertisement. The Secretary may retract or modify any prior comments the Secretary has provided with respect to the submitted advertisement based on new information or changed circumstances. The Secretary must provide written notice to the person of the new views and provide a reasonable time for modification or correction of an advertisement. The Secretary may compromise, modify, or remit, with or without conditions, any civil penalty.

New section 503B allows any person who requested a hearing and was ordered to pay a civil penalty to file a petition for de novo judicial review of such order with the United States Court of Appeals for the District of Columbia, or any other circuit in which such person resides or conducts business. A petition may only be filed within 60 days from the date the order making such assessments was issued.

New section 503B requires the Secretary to report to Congress on direct-to-consumer advertising and its ability to communicate to subsets of the general population, including elderly populations, children, and racial and ethnic minorities. The Secretary must establish a permanent advisory committee to advise the Secretary with respect to such report.

Section 902. Enforcement

Section 902 amends section 502 of the FFDCA to deem a drug misbranded if the sponsor fails to comply with a requirement of a REMS. This section amends section 303 of the FFDCA to establish civil penalties for violations of REMS requirements. Penalties would be not more than $250,000 for each violation, not to exceed $1 million for all violations adjudicated in one proceeding. If the violation continues after the applicant has been notified by the Secretary, penalties will not be more than $10 million per violation, not to exceed $50 million for all violations adjudicated in a single proceeding. If a violation continues and poses a threat to the public health, the Secretary may impose a penalty not to exceed $1 million per day.

Section 903. No effect on withdrawal or suspension of approval

Section 903 amends Section 505(e) of the FFDCA to make it clear that the Secretary is authorized to withdraw or suspend approval of an application without first ordering a REMS assessment.

Section 904. Benefit-risk assessments

Section 904 requires the FDA Commissioner to submit a report to Congress, within one year of enactment, on how best to communicate to the public the risks and benefits of new drugs, and the role of the REMS in assessing such risks and benefits.

Section 905. Postmarket risk identification and analysis system for active surveillance and assessment

Section 905 amends subsection 505(k) of the FFDCA to require the Secretary to establish public-private partnerships to develop tools and methods to enable the Secretary and others to use avail-

able electronic databases to create a robust surveillance system that will support active surveillance on important drug safety questions.

Section 905 requires the Secretary, in consultation with experts, to develop methods for integrating and analyzing safety data from multiple sources and mechanisms for obtaining access to that data within one year of enactment.

Section 905 requires the Secretary to have entered into partnerships that will allow the analysis of available data from the various data sources using developed standards and methods to identify drug safety signals and trends within two years of enactment.

Section 905 requires the Secretary to report to Congress on the ways in which the Secretary has used the surveillance system to identify specific drug safety signals and to better understand the outcomes associated with drugs marketed in the United States within four years of enactment.

Section 905 states disclosure of individually identifiable information, unless done lawfully, is prohibited in the surveillance system described in this subsection.

Proposed subparagraph 505(k)(7) indicates that entities may have other purposes for the use of databases other than the use described in this section, such as patient safety efforts or quality control. Nothing in this section prohibits lawful use or disclosure for such purposes. The Secretary has authority to interpret this paragraph and the term "disclosure" to allow entities that own a database to enter into contracts that allow contractors to access individually identifiable information in the database for the purpose of searches for the surveillance system, as long as the contract prohibits the contractor from disclosing individually identifiable information to which they have access through such activity.

Section 905 authorizes the use of PDUFA fees for the activities described in this section; and, in addition, authorizes appropriations of $25 million for each of FY2008 through FY2012 to carry out this section.

Section 905 requires that not later than 18 months after enactment, a GAO report shall evaluate data confidentiality and security issues relating to collection, transmission, and maintenance of data for the surveillance system established by this section. GAO shall also make recommendations to the Committees of jurisdiction regarding the need for any additional legislative or regulatory actions to ensure confidentiality and security of these data.

Section 907. Statement for inclusion in direct-to-consumer advertisements of drugs

Section 907 requires that direct-to-consumer advertisements include a statement encouraging individuals to report adverse effects of prescription drugs to FDA via the Internet (www.fda.gov/medwatch) or phone (1–800–FDA–1088).

Section 908. Clinical trial guidance for antibiotic drugs

Section 908 amends chapter V of the Federal Food, Drug, and Cosmetic Act by inserting after section 510 the following:

"Section 511. Clinical Trial Guidance for Antibiotic Drugs."

New section 511 states not later than one year after enactment of this section, the Secretary, acting through the Commissioner, shall issue guidance for the conduct of clinical trials with respect to antibiotic drugs. The guidelines shall indicate the appropriate animal models of infection, in vitro techniques, and valid microbiologic surrogate markers.

New section 511 requires, not later than five years after enactment, the Secretary, acting through the Commissioner, to review and update the guidance to reflect developments in scientific and medical information and technology.

Section 909. Prohibition against food to which drugs or biological products have been added

Section 909 amends section 301 of the Federal Food, Drug, and Cosmetic Act to prohibit the introduction or delivery for introduction into interstate commerce of any food to which a drug or biologic product is added unless the drug or biologic product was marketed in food before approval under section 505 of the FFDCA or section 351 of the PHSA.

Section 910. Assuring pharmaceutical safety

Section 910 amends Chapter V of the Federal Food, Drug, and Cosmetic Act by inserting after section 505B the following:

"Section 505C. Pharmaceutical Security."

New section 505C states the Secretary shall develop standards and identify and validate effective technologies for the purpose of securing the prescription drug distribution system against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs. In developing these standards, the Secretary shall consult with Federal health and security agencies, and address promising technologies.

The Committee urges the Secretary to take additional steps to further secure the pharmaceutical supply chain against the threat of counterfeit drugs. While there is no single solution to this growing threat, technology can enhance pharmaceutical security and frustrate the introduction of counterfeit products. As such, the Secretary should work to develop, recommend, and promote standards, in consultation with specified agencies and with industry stakeholders, including manufacturers, distributors, pharmacies, and third party standard-setting organizations, to encourage the development and adoption of anti-counterfeiting technologies.

New section 505C requires the Secretary to expand and enhance the resources and facilities of the Office of Regulatory Affairs of the Food and Drug Administration to protect the prescription drug distribution system, and establish regional capacities for the validation of prescription drugs and the inspection of the prescription drug distribution system.

Moreover, inspection and enforcement is essential to identify and punish criminals who seek to infiltrate the pharmaceutical supply chain. The Committee has therefore authorized additional appropriations to enhance joint enforcement activities and to coordinate inspections and enforcement wherever counterfeit products may be introduced. The Committee believes an inspection and enforcement

effort is necessary to properly confront this increasingly sophisticated threat to patient health and safety.

New section 505C defines the term prescription drug.

Section 911. Orphan antibiotic drugs

Section 911 states the Commissioner shall convene a public meeting regarding which serious and life threatening infectious diseases potentially qualify for available grants and contracts under section 5(a) of the Orphan Drug Act, regarding development of drugs for rare diseases.

Section 911 authorizes to be appropriated $30 million for each of fiscal years 2008 through 2012 for these purposes.

Section 912. Authorization of appropriations

Section 912 authorizes appropriations of $25 million for each of FY2008 through FY2012 for carrying out this title and amendments made by this title. This authorization of appropriations is in addition to other funds available for these activities.

Section 913. Effective date and applicability

Section 913 takes effect 180 days after enactment. A product with an approved application before the effective date of this Act is considered to have an approved REMS if there is: (1) a restriction on distribution or use under regulations for accelerated approval; or (2) an agreement between the Secretary and the applicant. Section 913 requires the sponsor to submit a proposed REMS to the Secretary within 180 days of enactment.

Section 913 grants the Secretary additional authorities for a product with an approved application before the effective date of this Act that does not have a restriction under accelerated approval regulations. The Secretary is authorized to require, on a case-by-case basis, that a sponsor submit a proposed REMS, in a specified timeframe, if the Secretary determines that its labeling may need modification, or another element of a REMS added. Section 913 authorizes the Secretary, in making such a requirement, to convene one or more FDA advisory committees to review a safety concern or dispute.

CHANGES IN EXISTING LAW MADE BY THE BILL, AS REPORTED

In compliance with clause 3(e) of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italic, existing law in which no change is proposed is shown in roman):

FEDERAL FOOD, DRUG, AND COSMETIC ACT

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CHAPTER III—PROHIBITED ACTS AND PENALTIES

PROHIBITED ACTS

SEC. 301. The following acts and the causing thereof are hereby prohibited:

(a) * * *

* * * * * * *

(jj) The dissemination of a television advertisement without complying with section 503B.

(kk) The introduction or delivery for introduction into interstate commerce of any food to which has been added—

(1) a drug approved under section 505,

(2) a biological product licensed under section 351 of the Public Health Service Act, or

(3) a drug or biological product for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public,

unless such drug or biological product was marketed in food before any approval of the drug under section 505 of this Act, before licensure of the biological product under section 351 of the Public Health Service Act, and before any substantial clinical investigations involving the drug or biological product have been instituted, or unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, approving the addition of such drug or biological product to the food.

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PENALTIES

SEC. 303. (a) * * *

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[(g)**]** *(f)*(1) * * *

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(2)(A) * * *

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(C) In a hearing to assess a civil penalty under this paragraph, the presiding officer shall have the same authority with regard to compelling testimony or production of documents as a presiding officer has under section 408(g)(2)(B). The third sentence of paragraph **[**(3)(A)**]** *(4)(A)* shall not apply to any investigation under this paragraph.

(3) Any applicant (as such term is used in section 505–1) who violates a requirement of section 505(o), section 505(p), or section 505–1 shall be subject to a civil monetary penalty of—

(A) not more than $250,000 per violation, and not to exceed $1,000,000 for all such violations adjudicated in a single proceeding; or

(B) in the case of a violation that continues after the Secretary provides notice of such violation to the applicant, not more than $10,000,000 per violation, and not to exceed $50,000,000 for all such violations adjudicated in a single proceeding.

If a violation referred to in subparagraph (A) or (B) is continuing in nature and poses a substantial threat to the public health, the Secretary may impose a civil penalty not to exceed $1,000,000 per day during such time period such person is in violation.

[(3)**]** *(4)*(A) A civil penalty under **[**paragraph (1) or (2)**]** *paragraph (1), (2), or (3)*shall be assessed by the Secretary by an order

made on the record after opportunity for a hearing provided in accordance with this subparagraph and section 554 of title 5, United States Code. Before issuing such an order, the Secretary shall give written notice to the person to be assessed a civil penalty under such order of the Secretary's proposal to issue such order and provide such person an opportunity for a hearing on the order. In the course of any investigation, the Secretary may issue subpoenas requiring the attendance and testimony of witnesses and the production of evidence that relates to the matter under investigation.

* * * * * * *

(C) The Secretary may compromise, modify, or remit, with or without conditions, any civil penalty which may be assessed under [paragraph (1) or (2)] *paragraph (1), (2), or (3)*. The amount of such penalty, when finally determined, or the amount agreed upon in compromise, may be deducted from any sums owing by the United States to the person charged.

[(4)] *(5)* Any person who requested, in accordance with paragraph (3)(A), a hearing respecting the assessment of a civil penalty and who is aggrieved by an order assessing a civil penalty may file a petition for judicial review of such order with the United States Court of Appeals for the District of Columbia Circuit or for any other circuit in which such person resides or transacts business. Such a petition may only be filed within the 60-day period beginning on the date the order making such assessment was issued.

[(5)] *(6)* If any person fails to pay an assessment of a civil penalty—

(A) after the order making the assessment becomes final, and if such person does not file a petition for judicial review of the order in accordance with paragraph [(4)] *(5)*, or

(B) after a court in an action brought under paragraph [(4)] *(5)* has entered a final judgment in favor of the Secretary,

the Attorney General shall recover the amount assessed (plus interest at currently prevailing rates from the date of the expiration of the 60-day period referred to in paragraph [(4)] *(5)* or the date of such final judgment, as the case may be) in an action brought in any appropriate district court of the United States. In such an action, the validity, amount, and appropriateness of such penalty shall not be subject to review.

(g)(1) With respect to a person who is a holder of an approved application under section 505 for a drug subject to section 503(b) or under section 351 of the Public Health Service Act, any such person who disseminates a direct-to-consumer advertisement that is false or misleading shall be liable to the United States for a civil penalty in an amount not to exceed $250,000 for the first such violation in any 3-year period, and not to exceed $500,000 for each subsequent violation in any 3-year period. No other civil monetary penalties in this Act (including the civil penalty in section 303(f)(3)) shall apply to a violation regarding direct-to-consumer advertising. For purposes of this paragraph: (A) Repeated dissemination of the same or similar advertisement prior to the receipt of the written notice referred to in paragraph (2) for such advertisements shall be considered one violation. (B) On and after the date of the receipt of such a notice, all violations under this paragraph occurring in a single day shall be considered one violation

(2) A civil penalty under paragraph (1) shall be assessed by the Secretary by an order made on the record after providing written notice to the person to be assessed a civil penalty and an opportunity for a hearing in accordance with this paragraph and section 554 of title 5, United States Code. If upon receipt of the written notice, the person to be assessed a civil penalty objects and requests a hearing, then in the course of any investigation related to such hearing, the Secretary may issue subpoenas requiring the attendance and testimony of witnesses and the production of evidence that relates to the matter under investigation, including information pertaining to the factors described in paragraph (3).

(3) Upon the request of the person to be assessed a civil penalty under paragraph (1), the Secretary, in determining the amount of the civil penalty, shall take into account the nature, circumstances, extent, and gravity of the violation or violations, including the following factors:

(A) Whether the person submitted the advertisement or a similar advertisement for review under section 736A.

(B) Whether the person submitted the advertisement for review if required under section 503B.

(C) Whether, after submission of the advertisement as described in subparagraph (A) or (B), the person disseminated the advertisement before the end of the 45-day comment period.

(D) Whether the person incorporated any comments made by the Secretary with regard to the advertisement into the advertisement prior to its dissemination.

(E) Whether the person ceased distribution of the advertisement upon receipt of the written notice referred to in paragraph (2) for such advertisement.

(F) Whether the person had the advertisement reviewed by qualified medical, regulatory, and legal reviewers prior to its dissemination.

(G) Whether the violations were material.

(H) Whether the person who created the advertisement acted in good faith.

(I) Whether the person who created the advertisement has been assessed a civil penalty under this provision within the previous 1-year period.

(J) The scope and extent of any voluntary, subsequent remedial action by the person.

(K) Such other matters, as justice may require.

(4)(A) Subject to subparagraph (B), no person shall be required to pay a civil penalty under paragraph (1) if the person submitted the advertisement to the Secretary and disseminated such advertisement after incorporating any comment received from the Secretary other than a recommendation subject to subsection 503B(c).

(B) The Secretary may retract or modify any prior comments the Secretary has provided to an advertisement submitted to the Secretary based on new information or changed circumstances, so long as the Secretary provides written notice to the person of the new views of the Secretary on the advertisement and provides a reasonable time for modification or correction of the advertisement prior to seeking any civil penalty under paragraph (1).

(5) The Secretary may compromise, modify, or remit, with or without conditions, any civil penalty which may be assessed under

paragraph (1). The amount of such penalty, when finally determined, or the amount charged upon in compromise, may be deducted from any sums owed by the United States to the person charged.

(6) Any person who requested, in accordance with paragraph (2), a hearing with respect to the assessment of a civil penalty and who is aggrieved by an order assessing a civil penalty, may file a petition for de novo judicial review of such order with the United States Court of Appeals for the District of Columbia Circuit or for any other circuit in which such person resides or transacts business. Such a petition may only be filed within the 60-day period beginning on the date the order making such assessments was issued.

(7) On an annual basis, the Secretary shall report to the Congress on direct-to-consumer advertising and its ability to communicate to subsets of the general population, including elderly populations, children, and racial and ethnic minority communities. The Secretary shall establish a permanent advisory committee to advise the Secretary with respect to such report. The membership of the advisory committee shall consist of nationally recognized medical, advertising, and communications experts, including experts representing subsets of the general population. The members of the advisory committee shall serve without pay, but may receive travel expenses, including per diem in lieu of subsistence in accordance with applicable provisions under subchapter I of chapter 57 of title 5, United States Code. The advisory committee shall study direct-to-consumer advertising as it relates to increased access to health information and decreased health disparities for these populations. The annual report required by this paragraph shall recommend effective ways to present and disseminate information to these populations. Such report shall also make recommendations regarding impediments to the participation of elderly populations, children, racially and ethnically diverse communities, and medically underserved populations in clinical drug trials and shall recommend best practice approaches for increasing the inclusion of such subsets of the general population. The Secretary shall submit the first annual report under this paragraph to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives not later than 18 months after the advisory committee has been convened by the Secretary.

(8) If any person fails to pay an assessment of a civil penalty under paragraph (1)—

(A) after the order making the assessment becomes final, and if such person does not file a petition for judicial review of the order in accordance with paragraph (6), or

(B) after a court in an action brought under paragraph (6) has entered a final judgment in favor of the Secretary,

the Attorney General of the United States shall recover the amount assessed (plus interest at currently prevailing rates from the date of the expiration of the 60-day period referred to in paragraph (6) or the date of such final judgment, as the case may be) in an action brought in any appropriate district court of the United States. In such an action, the validity, amount,

and appropriateness of such penalty shall not be subject to review.

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CHAPTER V—DRUGS AND DEVICES

SUBCHAPTER A—Drugs and Devices

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MISBRANDED DRUGS AND DEVICES

SEC. 502. A drug or device shall be deemed to be misbranded—
(a) * * *

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(n) In the case of any prescription drug distributed or offered for sale in any State, unless the manufacturer, packer, or distributor thereof includes in all advertisements and other descriptive printed matter issued or caused to be issued by the manufacturer, packer, or distributor with respect to that drug a true statement of (1) the established name as defined in section 502(e), printed prominently and in type at least half as large as that used for any trade or brand name thereof, (2) the formula showing quantitatively each ingredient of such drug to the extent required for labels under section 502(e), and (3) such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary in accordance with the procedure specified in section 701(e) [of this Act, except that] *of this Act, and in the case of any direct-to-consumer advertisement the following statement: "You are encouraged to report adverse effects of prescription drug medication to the FDA. Log onto www.fda.gov/medwatch or call 1–800–FDA–1088.", except that* (A) except in extraordinary circumstances, no regulation issued under this paragraph shall require prior approval by the Secretary of the content of any advertisement, and (B) no advertisement of a prescription drug, published after the effective date of regulations issued under this paragraph applicable to advertisements of prescription drugs, shall, with respect to the matters specified in this paragraph or covered by such regulations, be subject to the provisions of sections 12 through 17 of the Federal Trade Commission Act, as amended (15 U.S.C. 52–57). This paragraph (n) shall not be applicable to any printed matter which the Secretary determines to be labeling as defined in section 201(m) of this Act. Nothing in the Convention on Psychotropic Substances, signed at Vienna, Austria, on February 21, 1971, shall be construed to prevent drug price communications to consumers. *In the case of an advertisement for a drug subject to section 503(b)(1) presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear and conspicuous manner.*

* * * * * * *

(y) If it is a drug subject to an approved risk evaluation and mitigation strategy pursuant to section 505(p) and the person responsible for complying with the strategy fails to comply with a require-

ment of such strategy provided for under subsection (d), (e), or (f) of section 505–1.

(z) If it is a drug, and the responsible person (as such term is used in section 505(o)) is in violation of a requirement established under paragraph (3) (relating to postmarket studies and clinical trials) or paragraph (4) (relating to labeling) of section 505(o) with respect to such drug.

* * * * * * *

SEC. 503B. PREREVIEW OF TELEVISION ADVERTISEMENTS.

(a) IN GENERAL.—The Secretary may require the submission of any television advertisement for a drug (including any script, story board, rough, or a completed video production of the television advertisement) to the Secretary for review under this section not later than 45 days before dissemination of the television advertisement.

(b) REVIEW.—In conducting a review of a television advertisement under this section, the Secretary may make recommendations—

(1) on changes that are—

(A) necessary to protect the consumer good and well-being; or

(B) consistent with prescribing information for the product under review; and

(2) if appropriate and if information exists, on statements for inclusion in the advertisement to address the specific efficacy of the drug as it relates to a specific population group, including elderly populations, children, and racially and ethnically diverse populations.

(c) NO AUTHORITY TO REQUIRE CHANGES.—This section does not authorize the Secretary to make or direct changes in any material submitted pursuant to subsection (a).

(d) ELDERLY POPULATIONS, CHILDREN, RACIALLY AND ETHNICALLY DIVERSE COMMUNITIES.—In formulating recommendations under subsection (b), the Secretary shall take into consideration the impact of the advertised drug on elderly populations, children, and racially and ethnically diverse communities.

(e) SPECIFIC DISCLOSURES.—

(1) SERIOUS RISK; SAFETY PROTOCOL.—In conducting a review of a television advertisement under this section, if the Secretary determines that the advertisement would be false or misleading without a specific disclosure about a serious risk listed in the labeling of the drug involved, the Secretary may require inclusion of such disclosure in the advertisement.

(2) DATE OF APPROVAL.—In conducting a review of a television advertisement under this section, the Secretary may require the advertisement to include, for a period not to exceed 2 years from the date of the approval of the drug under section 505, a specific disclosure of such date of approval if the Secretary determines that the advertisement would otherwise be false or misleading.

(f) RULE OF CONSTRUCTION.—Nothing in this section may be construed as having any effect on the authority of the Secretary under section 314.550, 314.640, 601.45, or 601.94 of title 21, Code of Federal Regulations (or successor regulations).

* * * * * * *

NEW DRUGS

SEC. 505. (a) * * *

* * * * * * *

(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; *or (8) the applicant failed to submit the clinical trial information for any applicable clinical trial as required by section 492C of the Public Health Service Act;* he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that ❙clauses (1) through (6)❙ *paragraphs (1) through (8)* do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.

(e) The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the

basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided,* That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) or to comply with the notice requirements of section 510(k)(2), or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based. *The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit*

an assessment of the approved risk evaluation and mitigation strategy for the drug under section 505–1(g)(2)(D).

* * * * * * *

(i)(1) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(A) * * *

* * * * * * *

(C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b); **[**and**]**

(D) the submission to the Secretary by the manufacturer or the sponsor of the investigation of a new drug of a statement of intent regarding whether the manufacturer or sponsor has plans for assessing pediatric safety and efficacy**[**.**]***; and*

(E) the submission to the Director of NIH of clinical trial information for the clinical investigation at issue required under section 492C of the Public Health Service Act for inclusion in the registry database and the results database described in such section.

* * * * * * *

(3)(A) * * *

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; **[**or**]**

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before the date of the enactment of the Food and Drug Administration Modernization Act of 1997)**[**.**]***; or*

(iii) clinical trial information for the clinical investigation at issue was not submitted in compliance with section 492C of the Public Health Service Act.

* * * * * * *

(4) Regulations under paragraph (1) shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor

that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where it is not feasible or it is contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs. *The Secretary shall update such regulations to require inclusion in the informed consent form a statement that clinical trial information for such clinical investigation will be submitted for inclusion in the registry database and results database, as applicable, described in section 492C of the Public Health Service Act.*

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(k)(1) * * *

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(3) The Secretary shall establish public private partnerships to develop tools and methods to enable the Secretary and others to use available electronic databases to create a robust surveillance system that will support active surveillance on important drug safety questions including detecting and assessing drug safety signals; monitoring the frequency of known adverse events; and evaluating the outcomes of off label uses. Such surveillance shall provide for adverse event surveillance using the following data sources:

(A) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs).

(B) Private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data).

(C) Other information as the Secretary deems useful to create a robust system to identify and assess adverse events and potential drug safety signals and to evaluate the extent and outcomes of off label uses of drugs.

(4) Not later than 1 year after the date of the enactment of this paragraph, the Secretary, in consultation with experts including individuals who are recognized in the field of data privacy and security, shall develop methods for integrating and analyzing safety data from multiple sources and mechanisms for obtaining access to such data. Such methods and mechanisms shall not compromise the protection of individually identifiable health information.

(5) Not later than 2 years after the date of the enactment of this paragraph, the Secretary shall have entered into partnerships that will allow the analysis of available data from the various data sources using the standards and methods to identify drug safety signals and trends. Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

(6) Not later than 4 years after the date of the enactment of this paragraph, the Secretary shall report to the Congress on the ways in which the Secretary has used the surveillance system described in this subsection to identify specific drug safety signals and to bet-

ter understand the outcomes associated with drugs marketed in the United States.

(7) Disclosure of individually identifiable information is prohibited in the surveillance system described in this subsection. Nothing in this subsection prohibits lawful disclosure of such information for other purposes.

(8) Nothing in this subsection shall be construed as limiting public health activities authorized under law.

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(n)(1) * * *

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[(4) Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest requirement upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member's own scientific work is involved.**]**

[(5)**]** *(4)* The Secretary shall, as appropriate, provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this Act and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

[(6)**]** *(5)* Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS–15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, United States Code, for persons in the Government service employed intermittently.

[(7)**]** *(6)* The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such a panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meetings.

[(8)**]** *(7)* Within 90 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(o) POSTMARKET STUDIES AND CLINICAL TRIALS; LABELING.—

(1) IN GENERAL.—A responsible person may not introduce or deliver for introduction into interstate commerce the new drug

involved if the person is in violation of a requirement established under paragraph (3) or (4) with respect to the drug.

(2) DEFINITIONS.—For purposes of this subsection:

(A) RESPONSIBLE PERSON.—The term "responsible person" means a person who—

(i) has submitted to the Secretary a covered application that is pending; or

(ii) is the holder of an approved covered application.

(B) COVERED APPLICATION.—The term "covered application" means—

(i) an application under subsection (b) for a drug that is subject to section 503(b); and

(ii) an application under section 351 of the Public Health Service Act.

(C) NEW SAFETY INFORMATION; SERIOUS RISK.—The terms "new safety information", "serious risk", and "signal of a serious risk" have the meanings given such terms in section 505–1(b).

(3) STUDIES AND CLINICAL TRIALS.—

(A) IN GENERAL.—For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (C), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific information, including information regarding chemically-related or pharmacologically-related drugs.

(B) PURPOSES OF STUDY OR TRIAL.—The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

(i) To assess a known serious risk related to the use of the drug involved.

(ii) To assess signals of serious risk related to the use of the drug.

(iii) To identify a serious risk.

(C) ESTABLISHMENT OF REQUIREMENT AFTER APPROVAL OF COVERED APPLICATION.—The Secretary may require a postapproval study or studies or postapproval trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information. For each study required to be conducted under this subparagraph, the Secretary shall require that the applicant submit a timetable for completion of the study and shall require the applicant to periodically report to the Secretary on the status of the study. Unless the applicant demonstrates good cause for failure to comply with such timeline, the applicant shall be in violation of this subsection. The Secretary shall determine what constitutes good cause under the preceding sentence.

(4) SAFETY LABELING CHANGES REQUESTED BY SECRETARY.—

(A) NEW SAFETY INFORMATION.—The Secretary shall promptly notify the responsible person if the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug.

(B) RESPONSE TO NOTIFICATION.—Following notification pursuant to subparagraph (A), the responsible person shall within 30 days—

(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions; or

(ii) notify the Secretary that the responsible person does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

(C) REVIEW.—Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the responsible person's reasons why no labeling change is necessary, the Secretary shall initiate discussions with the responsible person to reach agreement on whether the labeling for the drug should be modified to reflect the new safety information, and if so, the contents of such labeling changes.

(D) DISCUSSIONS.—Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

(E) ORDER.—Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person to make such a labeling change as the Secretary deems appropriate to address the new safety information. Within 15 days of such an order, the responsible person shall submit a supplement containing the labeling change.

(F) DISPUTE RESOLUTION.—Within 5 days of receiving an order under subparagraph (E), the responsible person may appeal using the Food and Drug Administration's normal dispute resolution procedures established by the Secretary in regulation and guidance.

(G) VIOLATION.—If the change required by an order under subparagraph (E) is not made by the date so specified, the responsible person shall be considered to be in violation of this section.

(H) SERIOUS PUBLIC HEALTH THREAT.—Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that failure to make such a labeling change is necessary to protect against a serious public health threat, the Secretary may accelerate the timelines in such subparagraphs.

(I) RULE OF CONSTRUCTION.—This paragraph shall not be construed to affect the responsibility of the responsible person to maintain its label in accordance with existing requirements, including subpart B and section 314.70 of title 21, Code of Federal Regulations (or any successor regulations).

(p) RISK EVALUATION AND MITIGATION STRATEGY.—

(1) IN GENERAL.—A person may not introduce or deliver for introduction into interstate commerce a new drug if—

(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 503(b); or

(ii) the application for such drug is approved under section 351 of the Public Health Service Act; and

(B) a risk evaluation and mitigation strategy is required under section 505–1 with respect to the drug and—

(i) the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 505–1, including requirements regarding assessments of approved strategies; or

(ii) in the case of a requirement for such a strategy that is first established after the applicable application referred to in subparagraph (A) was approved with respect to the drug, the Secretary, after notice and opportunity for a hearing, publishes in the Federal Register a statement that the person is not cooperating with the Secretary in developing such a strategy for the drug.

(2) REQUIRED STATEMENT DURING APPROVAL PROCESS.—In the case of an application approved under subsection (b) or (j) for a new drug that is subject to section 503(b), or an application approved under section 351 of the Public Health Service Act, or a supplement to such an application that requires substantive data, the Secretary may not approve the application or supplement unless the person involved has complied with the following:

(A) The person has submitted to the Secretary a statement that provides the following information:

(i) Whether the person believes that a risk evaluation and mitigation strategy should be required under section 505–1.

(ii) Whether a postmarket study or clinical trial should be required under subsection (o)(3).

(B) In making the statement under subparagraph (A), the person took into account each of the following factors:

(i) The estimated size of the population likely to use the drug involved.

(ii) The seriousness of the disease or condition that is to be treated with the drug.

(iii) The expected benefit of the drug with respect to such disease or condition.

(iv) The expected or actual duration of treatment with the drug.

(v) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

(3) CERTAIN POSTMARKET STUDIES.—The failure to conduct a postmarket study under subpart H of part 314 of title 21, Code of Federal Regulations (or any successor regulation), is deemed to be a violation of paragraph (1).

SEC. 505–1. RISK EVALUATION AND MITIGATION STRATEGIES.

(a) SUBMISSION OF PROPOSED STRATEGY.—

(1) INITIAL APPROVAL.—A person who submits an application referred to in section 505(p)(1)(A) (referred to in this section as a "covered application") shall submit to the Secretary as part of

the application a proposed risk evaluation and mitigation strategy if the Secretary determines such a strategy is necessary to ensure that the benefits of the drug involved outweigh the risks of the drug. In making such a determination, the Secretary shall consider the statement submitted by the person under section 505(p)(2) with respect to the drug and shall consider the following factors:

(A) The estimated size of the population likely to use the drug involved.

(B) The seriousness of the disease or condition that is to be treated with the drug.

(C) The expected benefit of the drug with respect to such disease or condition.

(D) The expected or actual duration of treatment with the drug.

(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

(F) The availability and safety of a drug or other treatment, if any, for such disease or condition to which the safety of the drug may be compared.

(G) Whether the drug is a new molecular entity.

(2) POSTAPPROVAL REQUIREMENT.—

(A) IN GENERAL.—If the Secretary approves a covered application and does not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary may subsequently require such a strategy for the drug involved if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

(B) SUBMISSION OF PROPOSED STRATEGY.—Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other time as the Secretary requires to protect the public health, the holder shall submit to the Secretary a proposed risk evaluation and mitigation strategy.

(3) APPROVAL OF NEW INDICATION FOR USE.—The applicability of paragraph (2) includes applicability to a drug for which an approved covered application was in effect on the day before the effective date of this section and for which, on or after such effective date, the holder of the approved application submits to the Secretary a supplemental application seeking approval of a new indication for use of the drug.

(4) ABBREVIATED NEW DRUG APPLICATIONS.—The applicability of this section to an application under section 505(j) is subject to subsection (i).

(b) DEFINITIONS.—For purposes of this section:

(1) ADVERSE DRUG EXPERIENCE.—The term "adverse drug experience" means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

(A) an adverse event occurring in the course of the use of the drug in professional practice;

(B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;

(C) an adverse event occurring from abuse of the drug;

(D) an adverse event occurring from withdrawal of the drug; and

(E) any failure of expected pharmacological action of the drug.

(2) COVERED APPLICATION.—The term "covered application" has the meaning indicated for such term in subsection (a)(1).

(3) NEW SAFETY INFORMATION.—The term "new safety information" with respect to a drug means information about—

(A) a serious risk or an unexpected serious risk associated with use of the drug that the Secretary has become aware of since the drug was approved, since the risk evaluation and mitigation strategy was required, or since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or

(B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

(4) SERIOUS ADVERSE DRUG EXPERIENCE.—The term "serious adverse drug experience" is an adverse event that—

(A) results in—

(i) death;

(ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug experience that might have caused death had it occurred in a more severe form);

(iii) inpatient hospitalization or prolongation of existing hospitalization;

(iv) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or

(v) a congenital anomaly or birth defect; or

(B) based on appropriate medical judgment, may jeopardize the patient and may require a medical or surgical intervention to prevent an outcome described under subparagraph (A).

(5) SERIOUS RISK.—The term "serious risk" means a risk of a serious adverse drug experience.

(6) SIGNAL OF A SERIOUS RISK.—The term "signal of a serious risk" means information related to a serious adverse drug experience associated with use of a drug and derived from—

(A) a clinical trial;

(B) adverse event reports;

(C) a postapproval study, including a study under section 505(o)(3);

(D) peer-reviewed biomedical literature; or

(E) data derived from a postmarket risk identification and analysis system under section 505(k)(3).

(7) RESPONSIBLE PERSON.—The term "responsible person" has the meaning indicated for such term in subsection (e)(2).

(8) UNEXPECTED SERIOUS RISK.—The term "unexpected serious risk" means a serious adverse drug experience that is not listed in the labeling of a drug, or that may be symptomatically and pathophysiologically related to an adverse drug experience identified in the labeling, but differs from such adverse drug experience because of greater severity, specificity, or prevalence.

(c) CONTENTS.—A proposed risk evaluation and mitigation strategy under subsection (a) shall—

(1) include the timetable required under subsection (d); and

(2) to the extent required by the Secretary, include additional elements described in subsections (e) and (f).

(d) MINIMAL STRATEGY.—For purposes of subsection (c)(1), the risk evaluation and mitigation strategy for a drug shall require a timetable for submission of assessments of the strategy that—

(1) is not less frequent than once annually for the first 3 years after the strategy is initially approved;

(2) includes an assessment in the seventh year after the strategy is so approved; and

(3) subject to paragraph (2), for subsequent years—

(A) is at a frequency specified in the strategy;

(B) is increased or reduced in frequency as necessary as provided for in subsection (g)(4)(A); and

(C) is eliminated after the 3-year period described in paragraph (1) if the Secretary determines that serious risks of the drug have been adequately identified and assessed and are being adequately managed.

(e) ADDITIONAL POTENTIAL ELEMENTS OF STRATEGY.—

(1) IN GENERAL.—The Secretary may under subsection (c)(2) require that the risk evaluation and mitigation strategy for a drug include 1 or more of the additional elements described in this subsection if the Secretary makes the determination required with respect to the element involved.

(2) MEDGUIDE; PATIENT PACKAGE INSERT.—The risk evaluation and mitigation strategy for a drug may require that, as applicable, the person submitting the covered application or the holder of the approved such application (referred to in this section as the "responsible person") develop for distribution to each patient when the drug is dispensed—

(A) a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations); and

(B) a patient package insert, if the Secretary determines that such insert may help mitigate a serious risk of the drug.

(3) COMMUNICATION PLAN.—The risk evaluation and mitigation strategy for a drug may require that the responsible person conduct a communication plan to health care providers, if, with respect to such drug, the Secretary determines that such plan may support implementation of an element of the strategy. Such plan may include—

(A) sending letters to health care providers;

(B) disseminating information about the elements of the risk evaluation and mitigation strategy to encourage implementation by health care providers of components that apply to such health care providers, or to explain certain

safety protocols (such as medical monitoring by periodic laboratory tests); or

(C) disseminating information to health care providers through professional societies about any serious risks of the drug and any protocol to assure safe use.

(f) RESTRICTIONS ON DISTRIBUTION OR USE.—

(1) IN GENERAL.—If the Secretary determines that a drug shown to be effective can be safely used only if distribution or use of such drug is restricted, the Secretary may under subsection (c)(2) require as elements of the risk evaluation and mitigation strategy such restrictions on distribution or use as are needed to ensure safe use of the drug.

(2) ASSURING ACCESS AND MINIMIZING BURDEN.—Elements of a risk evaluation and mitigation strategy included under paragraph (1) shall—

(A) be commensurate with a specific serious risk listed in the labeling of the drug;

(B) be posted publicly by the Secretary with an explanation of how such elements will mitigate the observed safety risk, which posting shall be made within 30 days after the date on which the Secretary requires the element involved;

(C) considering the risk referred to in subparagraph (A), not be unduly burdensome on patient access to the drug, considering in particular—

(i) patients with serious or life-threatening diseases or conditions; and

(ii) patients who have difficulty accessing health care (such as patients in rural or medically underserved areas); and

(D) to the extent practicable, so as to minimize the burden on the health care delivery system—

(i) conform with elements to assure safe use for other drugs with similar, serious risks; and

(ii) be designed to be compatible with established distribution, procurement, and dispensing systems for drugs.

(3) ELEMENTS.—The restrictions on distribution or use described in paragraph (1) shall include 1 or more goals to evaluate or mitigate a serious risk listed in the labeling of the drug, and may require that—

(A) health care providers that prescribe the drug have special training or experience, or are specially certified, which training or certification with respect to the drug is available to any willing provider from a frontier area;

(B) pharmacies, practitioners, or health care settings that dispense the drug are specially certified, which training or certification with respect to the drug is available to any willing provider from a frontier area;

(C) the drug be dispensed to patients only in certain health care settings, such as hospitals;

(D) the drug be dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;

(E) each patient using the drug be subject to certain monitoring; or

(F) each patient using the drug be enrolled in a registry.

(4) IMPLEMENTATION SYSTEM.—The restrictions on distribution or use described in paragraph (1) may require a system through which the responsible person is able to—

(A) monitor and evaluate implementation of the restrictions by health care providers, pharmacists, patients, and other parties in the health care system who are responsible for implementing the restrictions;

(B) work to improve implementation of the restrictions by health care providers, pharmacists, patients, and other parties in the health care system who are responsible for implementing the restrictions; and

(C) notify wholesalers of the drug of those health care providers—

(i) who are responsible for implementing the restrictions; and

(ii) whom the responsible person knows have failed to meet their responsibilities for implementing the restrictions, after the responsible person has informed such party of such failure and such party has not remedied such failure.

(5) LIMITATION.—No holder of an approved application shall use any restriction on distribution required by the Secretary as necessary to assure safe use of the drug to block or delay approval of an application under section 505(b)(2) or (j) or to prevent application of such restriction under subsection (i)(1)(B) to a drug that is the subject of an abbreviated new drug application.

(6) BIOEQUIVALENCE TESTING.—Notwithstanding any other provisions in this subsection, the holder of an approved application that is subject to distribution restrictions required under this subsection that limit the ability of a sponsor seeking approval of an application under subsection 505(b)(2) or (j) to purchase on the open market a sufficient quantity of drug to conduct bioequivalence testing shall provide to such a sponsor a sufficient amount of drug to conduct bioequivalence testing if the sponsor seeking approval under section 505(b)(2) or (j)—

(A) agrees to such restrictions on distribution as the Secretary finds necessary to assure safe use of the drug during bioequivalence testing; and

(B) pays the holder of the approved application the fair market value of the drug purchased for bioequivalence testing.

(7) LETTER BY SECRETARY.—Upon a showing by the sponsor seeking approval under section 505(b)(2) or (j) that the sponsor has agreed to such restrictions necessary to assure safe use of the drug during bioequivalence testing, the Secretary shall issue to the sponsor seeking to conduct bioequivalence testing a letter that describes the Secretary's finding which shall serve as proof that the sponsor has satisfied the requirements of subparagraph (6)(A).

(8) EVALUATION OF ELEMENTS TO ASSURE SAFE USE.—The Secretary, acting through the Drug Safety and Risk Manage-

ment Advisory Committee (or any successor committee) of the Food and Drug Administration, shall—

(A) seek input from patients, physicians, pharmacists, and other health care providers about how elements to assure safe use under this subsection for 1 or more drugs may be standardized so as not to be—

(i) unduly burdensome on patient access to the drug; and

(ii) to the extent practicable, minimize the burden on the health care delivery system;

(B) at least annually, evaluate, for 1 or more drugs, the elements to assure safe use of such drug to assess whether the elements—

(i) assure safe use of the drug;

(ii) are not unduly burdensome on patient access to the drug; and

(iii) to the extent practicable, minimize the burden on the health care delivery system; and

(C) considering such input and evaluations—

(i) issue or modify agency guidance about how to implement the requirements of this subsection; and

(ii) modify elements under this subsection for 1 or more drugs as appropriate.

(9) WAIVER IN PUBLIC HEALTH EMERGENCIES.—The Secretary may waive any restriction on distribution or use under this subsection during the period described in section 319(a) of the Public Health Service Act with respect to a qualified countermeasure described under section 319F–1(a)(2) of such Act, to which a restriction or use under this subsection has been applied, if the Secretary has—

(A) declared a public health emergency under such section 319; and

(B) determined that such waiver is required to mitigate the effects of, or reduce the severity of, such public health emergency.

(g) ASSESSMENT AND MODIFICATION OF APPROVED STRATEGY.—

(1) VOLUNTARY ASSESSMENTS.—After the approval of a risk evaluation and mitigation strategy under subsection (a), the responsible person involved may, subject to paragraph (2), submit to the Secretary an assessment of, and propose a modification to, the approved strategy for the drug involved at any time.

(2) REQUIRED ASSESSMENTS.—A responsible person shall, subject to paragraph (5), submit an assessment of, and may propose a modification to, the approved risk evaluation and mitigation strategy for a drug—

(A) when submitting a supplemental application for a new indication for use under section 505(b) or under section 351 of the Public Health Service Act, unless the drug is not subject to section 503(b) and the risk evaluation and mitigation strategy for the drug includes only the timetable under subsection (d);

(B) when required by the strategy, as provided for in such timetable under subsection (d);

(C) within a time period to be determined by the Secretary, if the Secretary determines that new safety or effectiveness information indicates that—

(i) an element under subsection (d) or (e) should be modified or included in the strategy; or

(ii) an element under subsection (f) should be modified or included in the strategy; or

(D) within 15 days when ordered by the Secretary, if the Secretary determines that there may be a cause for action by the Secretary under section 505(e).

(3) REQUIREMENTS FOR ASSESSMENTS.—An assessment under paragraph (1) or (2) of an approved risk evaluation and mitigation strategy for a drug shall include—

(A) with respect to any goal under subsection (f), an assessment of the extent to which the restrictions on distribution or use are meeting the goal or whether the goal or such restrictions should be modified;

(B) with respect to any postapproval study required under section 505(o)(3), the status of such study, including whether any difficulties completing the study have been encountered; and

(C) with respect to any postapproval clinical trial required under section 505(o), the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under section 492C of the Public Health Service Act.

(4) MODIFICATION.—A modification (whether an enhancement or a reduction) to the approved risk evaluation and mitigation strategy for a drug may include the addition or modification of any element under subsection (d) or the addition, modification, or removal of any element under subsection (e) or (f), such as—

(A) modifying the timetable for assessments of the strategy under subsection (d), including to eliminate assessments; or

(B) adding, modifying, or removing a restriction on distribution or use under subsection (f).

(5) NO EFFECT ON LABELING CHANGES THAT DO NOT REQUIRE PREAPPROVAL.—In the case of a labeling change to which section 314.70 of title 21, Code of Federal Regulations (or any successor regulation), applies for which the submission of a supplemental application is not required or for which distribution of the drug involved may commence upon the receipt by the Secretary of a supplemental application for the change, the submission of an assessment of the approved risk evaluation and mitigation strategy for the drug under paragraph (2) is not required.

(h) REVIEW OF PROPOSED STRATEGIES; REVIEW OF ASSESSMENTS OF APPROVED STRATEGIES.—

(1) IN GENERAL.—The Secretary shall promptly review each proposed risk evaluation and mitigation strategy for a drug submitted under subsection (a) and each assessment of an ap-

proved risk evaluation and mitigation strategy for a drug submitted under subsection (g).

(2) MARKETING PLAN.—As part of a review conducted under this subsection, the Secretary may require the applicant to submit information regarding its marketing plan and practices for the drug, so as to allow the Secretary to determine whether any of the proposed or ongoing marketing activities undermine any of the requirements of the risk evaluation and mitigation strategy.

(3) DISCUSSION.—The Secretary shall initiate discussions with a responsible person for purposes of this subsection to determine a strategy—

(A) if the proposed strategy is submitted as part of an application or supplemental application under subsection (a) or subsection (g)(2)(A), not less than 60 days before the action deadline for the application that has been agreed to by the Secretary and that has been set forth in goals identified in letters of the Secretary (relating to the use of fees collected under section 736 to expedite the drug development process and the process for the review of human drug applications);

(B) if the assessment is submitted under subparagraph (B) or (C) or subsection (g)(2), not later than 20 days after such submission;

(C) if the assessment is submitted under subsection (g)(1) or subsection (g)(2)(D) , not later than 30 days after such submission; or

(D) if the assessment is submitted under subsection (g)(2)(D), not later than 10 days after such submission.

(4) ACTION.—

(A) IN GENERAL.—Unless the responsible person requests the dispute resolution process described under paragraph (5), the Secretary shall approve and describe the risk evaluation and mitigation strategy for a drug, or any modification to the strategy—

(i) as part of the action letter on the application, when a proposed strategy is submitted under subsection (a) or an assessment of the strategy is submitted under subsection (g)(1); or

(ii) in an order issued not later than 50 days after the date discussions of such modification begin under paragraph (3), when an assessment of the strategy is submitted under subsection (g)(1) or under any of subparagraphs (B) through (D) of subsection (g)(2).

(B) INACTION.—An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided under subparagraph (A).

(C) PUBLIC AVAILABILITY.—Any action letter described in subparagraph (A)(i) or order described in subparagraph (A)(ii) shall be made publicly available.

(5) DISPUTE RESOLUTION.—

(A) REQUEST FOR REVIEW.—

(i) IN GENERAL.—Not earlier than 15 days, and not later than 35 days, after discussions under paragraph

(3) have begun, the responsible person may request in writing that a dispute about the strategy be reviewed by the Drug Safety Oversight Board under subsection (j), except that the determination of the Secretary to require a risk evaluation and mitigation strategy is not subject to review under this paragraph. The preceding sentence does not prohibit review under this paragraph of the particular elements of such a strategy.

(ii) SCHEDULING.—Upon receipt of a request under clause (i), the Secretary shall schedule the dispute involved for review under subparagraph (B) and, not later than 5 business days of scheduling the dispute for review, shall publish by posting on the Internet or otherwise a notice that the dispute will be reviewed by the Drug Safety Oversight Board.

(B) SCHEDULING REVIEW.—If a responsible person requests review under subparagraph (A), the Secretary—

(i) shall schedule the dispute for review at 1 of the next 2 regular meetings of the Drug Safety Oversight Board, whichever meeting date is more practicable; or

(ii) may convene a special meeting of the Drug Safety Oversight Board to review the matter more promptly, including to meet an action deadline on an application (including a supplemental application).

(C) AGREEMENT AFTER DISCUSSION OR ADMINISTRATIVE APPEALS.—

(i) FURTHER DISCUSSION OR ADMINISTRATIVE APPEALS.—A request for review under subparagraph (A) shall not preclude further discussions to reach agreement on the risk evaluation and mitigation strategy, and such a request shall not preclude the use of administrative appeals within the Food and Drug Administration to reach agreement on the strategy, including appeals as described in letters of the Secretary (relating to the use of fees collected under section 736 to expedite the drug development process and the process for the review of human drug applications) for procedural or scientific matters involving the review of human drug applications and supplemental applications that cannot be resolved at the divisional level.

(ii) AGREEMENT TERMINATES DISPUTE RESOLUTION.—At any time before a decision and order is issued under subparagraph (G) , the Secretary and the responsible person may reach an agreement on the risk evaluation and mitigation strategy through further discussion or administrative appeals, terminating the dispute resolution process, and the Secretary shall issue an action letter or order, as appropriate, that describes the strategy.

(D) MEETING OF THE BOARD.—At a meeting of the Drug Safety Oversight Board described in subparagraph (B), the Board shall—

(i) hear from both parties; and

(ii) review the dispute.

(E) RECORD OF PROCEEDINGS.—The Secretary shall ensure that the proceedings of any such meeting are recorded, transcribed, and made public within 30 days of the meeting. The Secretary shall redact the transcript to protect any trade secrets or other confidential information described in section 552(b)(4) of title 5, United States Code.

(F) RECOMMENDATION OF THE BOARD.—Not later than 5 days after any such meeting, the Drug Safety Oversight Board shall provide a written recommendation on resolving the dispute to the Secretary. Not later than 5 days after the Board provides such written recommendation to the Secretary, the Secretary shall make the recommendation available to the public.

(G) ACTION BY THE SECRETARY.—

(i) ACTION LETTER.—With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall issue an action letter that resolves the dispute not later than the later of—

(I) the action deadline referred to in paragraph (3)(A); or

(II) 7 days after receiving the recommendation of the Drug Safety Oversight Board.

(ii) ORDER.—With respect to an assessment of an approved risk evaluation and mitigation strategy under subsection (g)(1) or under any of subparagraphs (B) through (D) of subsection (g)(2), the Secretary shall issue an order, which shall be made public, that resolves the dispute not later than 7 days after receiving the recommendation of the Drug Safety Oversight Board.

(H) INACTION.—An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided for under subparagraph (G).

(I) EFFECT ON ACTION DEADLINE.—With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall be considered to have met the action deadline referred to in paragraph (3)(A) with respect to the application involved if the responsible person requests the dispute resolution process described in this paragraph and if the Secretary—

(i) has initiated the discussions described under paragraph (3) not less than 60 days before such action deadline; and

(ii) has complied with the timing requirements of scheduling review by the Drug Safety Oversight Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.

(J) DISQUALIFICATION.—No individual who is an employee of the Food and Drug Administration and who reviews a drug or who participated in an administrative appeal under subparagraph (C)(i) with respect to such drug may serve on the Drug Safety Oversight Board at a meeting

under subparagraph (D) to review a dispute about the risk evaluation and mitigation strategy for such drug.

(K) ADDITIONAL EXPERTISE.—The Drug Safety Oversight Board may add members with relevant expertise from the Food and Drug Administration, including the Office of Pediatrics, the Office of Women's Health, or the Office of Rare Diseases, or from other Federal public health or health care agencies, for a meeting under subparagraph (D) of the Drug Safety Oversight Board.

(6) USE OF ADVISORY COMMITTEES.—The Secretary may convene a meeting of 1 or more advisory committees of the Food and Drug Administration to—

(A) review a concern about the safety of a drug or class of drugs, including before an assessment of the risk evaluation and mitigation strategy or strategies of such drug or drugs is required to be submitted under any of subparagraphs (B) through (D) of subsection (g)(2);

(B) review the risk evaluation and mitigation strategy or strategies of a drug or group of drugs; or

(C) review a dispute under paragraph (5).

(7) PROCESS FOR ADDRESSING DRUG CLASS EFFECTS.—

(A) IN GENERAL.—When a concern about a serious risk of a drug may be related to the pharmacological class of the drug, the Secretary may defer assessments of the approved risk evaluation and mitigation strategies for such drugs until the Secretary has convened 1 or more public meetings to consider possible responses to such concern. If the Secretary defers an assessment under this subparagraph, the Secretary shall give notice to the public of the deferral not later than 5 days of the deferral.

(B) PUBLIC MEETINGS.—Such public meetings may include—

(i) 1 or more meetings of the reviewed entities for such drugs;

(ii) 1 or more meetings of 1 or more advisory committees of the Food and Drug Administration, as provided for under paragraph (6); or

(iii) 1 or more workshops of scientific experts and other stakeholders.

(C) ACTION.—After considering the discussions from any meetings under subparagraph (B), the Secretary may—

(i) announce in the Federal Register a planned regulatory action, including a modification to each risk evaluation and mitigation strategy, for drugs in the pharmacological class;

(ii) seek public comment about such action; and

(iii) after seeking such comment, issue an order addressing such regulatory action.

(8) INTERNATIONAL COORDINATION.—The Secretary may coordinate the timetable for submission of assessments under subsection (d), or a study or clinical trial under section 505(o)(3), with efforts to identify and assess the serious risks of such drug by the marketing authorities of other countries whose drug approval and risk management processes the Secretary deems comparable to the drug approval and risk management proc-

esses of the United States. If the Secretary takes action to coordinate such timetable, the Secretary shall give notice to the public of the action not later than 5 days after the action.

(9) EFFECT.—Use of the processes described in paragraphs (7) and (8) shall not delay action on an application or a supplement to an application for a drug.

(i) ABBREVIATED NEW DRUG APPLICATIONS.—

(1) IN GENERAL.—A drug that is the subject of an abbreviated new drug application under section 505(j) is subject to only the following elements of the risk evaluation and mitigation strategy required under subsection (a) for the applicable listed drug:

(A) A Medication Guide or patient package insert, if required under subsection (e) for the applicable listed drug.

(B) Restrictions on distribution or use, if required under subsection (f) for the listed drug. A drug that is the subject of an abbreviated new drug application and the listed drug shall use a single, shared system under subsection (f)(4). The Secretary may waive the requirement under the preceding sentence for a drug that is the subject of an abbreviated new drug application if the Secretary determines that—

(i) it is not practical for the drug to use such single, shared system; or

(ii) the burden of using the single, shared system outweighs the benefit of using the single system.

(2) ACTION BY SECRETARY.—For an applicable listed drug for which a drug is approved under section 505(j), the Secretary—

(A) shall undertake any communication plan to health care providers required under subsection (e)(3) for the applicable listed drug; and

(B) shall inform the responsible person for the drug that is so approved if the risk evaluation and mitigation strategy for the applicable listed drug is modified.

(j) DRUG SAFETY OVERSIGHT BOARD.—

(1) IN GENERAL.—There is established a Drug Safety Oversight Board.

(2) COMPOSITION; MEETINGS.—The Drug Safety Oversight Board shall—

(A) be composed of scientists and health care practitioners appointed by the Secretary, each of whom is an employee of the Federal Government;

(B) include representatives from offices throughout the Food and Drug Administration;

(C) include at least 1 representative from each of the National Institutes of Health and the Department of Health and Human Services (other than the Food and Drug Administration);

(D) include such representatives as the Secretary shall designate from other appropriate agencies that wish to provide representatives; and

(E) meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.

[SEC. 505A. PEDIATRIC STUDIES OF DRUGS.

[(a) DEFINITIONS.—As used in this section, the term "pediatric studies" or "studies" means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used.

[(b) MARKET EXCLUSIVITY FOR NEW DRUGS.—If, prior to approval of an application that is submitted under section 505(b)(1), the Secretary determines that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), and such studies are completed within any such timeframe and the reports thereof submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)—

[(1)(A)(i) the period referred to in subsection (c)(3)(D)(ii) of section 505, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

[(ii) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

[(B) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

[(2)(A) if the drug is the subject of—

[(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

[(ii) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

[(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

[(c) MARKET EXCLUSIVITY FOR ALREADY-MARKETED DRUGS.—If the Secretary determines that information relating to the use of an approved drug in the pediatric population may produce health ben-

efits in that population and makes a written request to the holder of an approved application under section 505(b)(1) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, the studies are completed within any such timeframe, and the reports thereof are submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)—

[(1)(A)(i) the period referred to in subsection (c)(3)(D)(ii) of section 505, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

[(ii) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

[(B) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

[(2)(A) if the drug is the subject of—

[(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

[(ii) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

[(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

[(d) CONDUCT OF PEDIATRIC STUDIES.—

[(1) AGREEMENT FOR STUDIES.—The Secretary may, pursuant to a written request from the Secretary under subsection (b) or (c), after consultation with—

[(A) the sponsor of an application for an investigational new drug under section 505(i);

[(B) the sponsor of an application for a new drug under section 505(b)(1); or

[(C) the holder of an approved application for a drug under section 505(b)(1),

agree with the sponsor or holder for the conduct of pediatric studies for such drug. Such agreement shall be in writing and shall include a timeframe for such studies.

[(2) WRITTEN PROTOCOLS TO MEET THE STUDIES REQUIREMENT.—If the sponsor or holder and the Secretary agree upon written protocols for the studies, the studies requirement of subsection (b) or (c) is satisfied upon the completion of the studies and submission of the reports thereof in accordance with the original written request and the written agreement referred to in paragraph (1). In reaching an agreement regarding written protocols, the Secretary shall take into account adequate representation of children of ethnic and racial minorities. Not later than 60 days after the submission of the report of the studies, the Secretary shall determine if such studies were or were not conducted in accordance with the original written request and the written agreement and reported in accordance with the requirements of the Secretary for filing and so notify the sponsor or holder.

[(3) OTHER METHODS TO MEET THE STUDIES REQUIREMENT.—If the sponsor or holder and the Secretary have not agreed in writing on the protocols for the studies, the studies requirement of subsection (b) or (c) is satisfied when such studies have been completed and the reports accepted by the Secretary. Not later than 90 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 90 days, whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing.

[(4) WRITTEN REQUEST TO HOLDERS OF APPROVED APPLICATIONS FOR DRUGS THAT HAVE MARKET EXCLUSIVITY.—

[(A) REQUEST AND RESPONSE.—If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (c) to the holder of an application approved under section 505(b)(1), the holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the holder to act on the request by—

[(i) indicating when the pediatric studies will be initiated, if the holder agrees to the request; or

[(ii) indicating that the holder does not agree to the request.

[(B) NO AGREEMENT TO REQUEST.—

[(i) REFERRAL.—If the holder does not agree to a written request within the time period specified in subparagraph (A), and if the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall refer the drug to the Foundation for the National Institutes of Health established under section 499 of the Public Health Service Act (42 U.S.C. 290b) (re-

ferred to in this paragraph as the "Foundation") for the conduct of the pediatric studies described in the written request.

[(ii) PUBLIC NOTICE.—The Secretary shall give public notice of the name of the drug, the name of the manufacturer, and the indications to be studied made in a referral under clause (i).

[(C) LACK OF FUNDS.—On referral of a drug under subparagraph (B)(i), the Foundation shall issue a proposal to award a grant to conduct the requested studies unless the Foundation certifies to the Secretary, within a timeframe that the Secretary determines is appropriate through guidance, that the Foundation does not have funds available under section 499(j)(9)(B)(i) to conduct the requested studies. If the Foundation so certifies, the Secretary shall refer the drug for inclusion on the list established under section 409I of the Public Health Service Act for the conduct of the studies.

[(D) EFFECT OF SUBSECTION.—Nothing in this subsection (including with respect to referrals from the Secretary to the Foundation) alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

[(E) NO REQUIREMENT TO REFER.—Nothing in this subsection shall be construed to require that every declined written request shall be referred to the Foundation.

[(F) WRITTEN REQUESTS UNDER SUBSECTION (b).—For drugs under subsection (b) for which written requests have not been accepted, if the Secretary determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall issue a written request under subsection (c) after the date of approval of the drug.

[(e) DELAY OF EFFECTIVE DATE FOR CERTAIN APPLICATION.—If the Secretary determines that the acceptance or approval of an application under section 505(b)(2) or 505(j) for a new drug may occur after submission of reports of pediatric studies under this section, which were submitted prior to the expiration of the patent (including any patent extension) or the applicable period under clauses (ii) through (iv) of section 505(c)(3)(D) or clauses (ii) through (iv) of section 505(j)(5)(F), but before the Secretary has determined whether the requirements of subsection (d) have been satisfied, the Secretary shall delay the acceptance or approval under section 505(b)(2) or 505(j) until the determination under subsection (d) is made, but any such delay shall not exceed 90 days. In the event that requirements of this section are satisfied, the applicable six-month period under subsection (b) or (c) shall be deemed to have been running during the period of delay.

[(f) NOTICE OF DETERMINATIONS ON STUDIES REQUIREMENT.—The Secretary shall publish a notice of any determination that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 505 for a drug will be subject to the provisions of this section.

[(g) LIMITATIONS.—A drug to which the six-month period under subsection (b) or (c) has already been applied—

[(1) may receive an additional six-month period under subsection (c)(1)(A)(ii) for a supplemental application if all other requirements under this section are satisfied, except that such a drug may not receive any additional such period under subsection (c)(2); and

[(2) may not receive any additional such period under subsection (c)(1)(B).

[(h) RELATIONSHIP TO PEDIATRIC RESEARCH REQUIREMENTS.—Notwithstanding any other provision of law, if any pediatric study is required by a provision of law (including a regulation) other than this section and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.

[(i) LABELING SUPPLEMENTS.—

[(1) PRIORITY STATUS FOR PEDIATRIC SUPPLEMENTS.—Any supplement to an application under section 505 proposing a labeling change pursuant to a report on a pediatric study under this section—

[(A) shall be considered to be a priority supplement; and

[(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

[(2) DISPUTE RESOLUTION.—

[(A) REQUEST FOR LABELING CHANGE AND FAILURE TO AGREE.—If the Commissioner determines that an application with respect to which a pediatric study is conducted under this section is approvable and that the only open issue for final action on the application is the reaching of an agreement between the sponsor of the application and the Commissioner on appropriate changes to the labeling for the drug that is the subject of the application, not later than 180 days after the date of submission of the application—

[(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

[(ii) if the sponsor of the application does not agree to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

[(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

[(i) review the pediatric study reports; and

[(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

[(C) CONSIDERATION OF RECOMMENDATIONS.—The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling change that the Commissioner determines to be appropriate.

[(D) MISBRANDING.—If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded.

[(E) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under this Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

[(j) DISSEMINATION OF PEDIATRIC INFORMATION.—

[(1) IN GENERAL.—Not later than 180 days after the date of submission of a report on a pediatric study under this section, the Commissioner shall make available to the public a summary of the medical and clinical pharmacology reviews of pediatric studies conducted for the supplement, including by publication in the Federal Register.

[(2) EFFECT OF SUBSECTION.—Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

[(k) CLARIFICATION OF INTERACTION OF MARKET EXCLUSIVITY UNDER THIS SECTION AND MARKET EXCLUSIVITY AWARDED TO AN APPLICANT FOR APPROVAL OF A DRUG UNDER SECTION 505(j).—If a 180-day period under section 505(j)(5)(B)(iv) overlaps with a 6-month exclusivity period under this section, so that the applicant for approval of a drug under section 505(j) entitled to the 180-day period under that section loses a portion of the 180-day period to which the applicant is entitled for the drug, the 180-day period shall be extended from—

[(1) the date on which the 180-day period would have expired by the number of days of the overlap, if the 180-day period would, but for the application of this subsection, expire after the 6-month exclusivity period; or

[(2) the date on which the 6-month exclusivity period expires, by the number of days of the overlap if the 180-day period would, but for the application of this subsection, expire during the six-month exclusivity period.

[(l) PROMPT APPROVAL OF DRUGS UNDER SECTION 505(j) WHEN PEDIATRIC INFORMATION IS ADDED TO LABELING.—

[(1) GENERAL RULE.—A drug for which an application has been submitted or approved under section 505(j) shall not be considered ineligible for approval under that section or misbranded under section 502 on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity under clause (iii) or (iv) of section 505(j)(5)(F).

[(2) LABELING.—Notwithstanding clauses (iii) and (iv) of section 505(j)(5)(F), the Secretary may require that the labeling of a drug approved under section 505(j) that omits a pediatric in-

dication or other aspect of labeling as described in paragraph (1) include—

[(A) a statement that, because of marketing exclusivity for a manufacturer—

[(i) the drug is not labeled for pediatric use; or

[(ii) in the case of a drug for which there is an additional pediatric use not referred to in paragraph (1), the drug is not labeled for the pediatric use under paragraph (1); and

[(B) a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary.

[(3) PRESERVATION OF PEDIATRIC EXCLUSIVITY AND OTHER PROVISIONS.—This subsection does not affect—

[(A) the availability or scope of exclusivity under this section;

[(B) the availability or scope of exclusivity under section 505 for pediatric formulations;

[(C) the question of the eligibility for approval of any application under section 505(j) that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of section 505(j)(5)(F); or

[(D) except as expressly provided in paragraphs (1) and (2), the operation of section 505.

[(m) REPORT.—The Secretary shall conduct a study and report to Congress not later than January 1, 2001, based on the experience under the program established under this section. The study and report shall examine all relevant issues, including—

[(1) the effectiveness of the program in improving information about important pediatric uses for approved drugs;

[(2) the adequacy of the incentive provided under this section;

[(3) the economic impact of the program on taxpayers and consumers, including the impact of the lack of lower cost generic drugs on patients, including on lower income patients; and

[(4) any suggestions for modification that the Secretary determines to be appropriate.

[(n) SUNSET.—A drug may not receive any 6-month period under subsection (a) or (c) unless—

[(1) on or before October 1, 2007, the Secretary makes a written request for pediatric studies of the drug;

[(2) on or before October 1, 2007, an application for the drug is accepted for filing under section 505(b); and

[(3) all requirements of this section are met.

[SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.

[(a) NEW DRUGS AND BIOLOGICAL PRODUCTS.—

[(1) IN GENERAL.—A person that submits an application (or supplement to an application)—

[(A) under section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration; or

[(B) under section 351 of the Public Health Service Act (42 U.S.C. 262) for a new active ingredient, new indication,

new dosage form, new dosing regimen, or new route of administration;

shall submit with the application the assessments described in paragraph (2).

[(2) ASSESSMENTS.—

[(A) IN GENERAL.—The assessments referred to in paragraph (1) shall contain data, gathered using appropriate formulations for each age group for which the assessment is required, that are adequate—

[(i) to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations; and

[(ii) to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective.

[(B) SIMILAR COURSE OF DISEASE OR SIMILAR EFFECT OF DRUG OR BIOLOGICAL PRODUCT.—

[(i) IN GENERAL.—If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies.

[(ii) EXTRAPOLATION BETWEEN AGE GROUPS.—A study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group.

[(3) DEFERRAL.—On the initiative of the Secretary or at the request of the applicant, the Secretary may defer submission of some or all assessments required under paragraph (1) until a specified date after approval of the drug or issuance of the license for a biological product if—

[(A) the Secretary finds that—

[(i) the drug or biological product is ready for approval for use in adults before pediatric studies are complete;

[(ii) pediatric studies should be delayed until additional safety or effectiveness data have been collected; or

[(iii) there is another appropriate reason for deferral; and

[(B) the applicant submits to the Secretary—

[(i) certification of the grounds for deferring the assessments;

[(ii) a description of the planned or ongoing studies; and

[(iii) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time.

[(4) WAIVERS.—

[(A) FULL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this

subsection if the applicant certifies and the Secretary finds that—

[(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients is so small or the patients are geographically dispersed);

[(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups; or

[(iii) the drug or biological product—

[(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

[(II) is not likely to be used in a substantial number of pediatric patients.

[(B) PARTIAL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

[(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

[(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

[(iii) the drug or biological product—

[(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

[(II) is not likely to be used by a substantial number of pediatric patients in that age group; or

[(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

[(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation.

[(D) LABELING REQUIREMENT.—If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

[(b) MARKETED DRUGS AND BIOLOGICAL PRODUCTS.—

[(1) IN GENERAL.—After providing notice in the form of a letter and an opportunity for written response and a meeting, which may include an advisory committee meeting, the Secretary may (by order in the form of a letter) require the holder of an approved application for a drug under section 505 or the holder of a license for a biological product under section 351 of the Public Health Service Act (42 U.S.C. 262) to submit by a

specified date the assessments described in subsection (a)(2) if the Secretary finds that—

[(A)(i) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and

[(ii) the absence of adequate labeling could pose significant risks to pediatric patients; or

[(B)(i) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for one or more of the claimed indications; and

[(ii) the absence of adequate labeling could pose significant risks to pediatric patients.

[(2) WAIVERS.—

[(A) FULL WAIVER.—At the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments under this subsection if the applicant certifies and the Secretary finds that—

[(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed); or

[(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups.

[(B) PARTIAL WAIVER.—At the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

[(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

[(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

[(iii)(I) the drug or biological product—

[(aa) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

[(bb) is not likely to be used in a substantial number of pediatric patients in that age group; and

[(II) the absence of adequate labeling could not pose significant risks to pediatric patients; or

[(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

[(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation.

[(D) LABELING REQUIREMENT.—If the Secretary grants a full or partial waiver because there is evidence that a drug

or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

[(3) RELATIONSHIP TO OTHER PEDIATRIC PROVISIONS.—

[(A) NO ASSESSMENT WITHOUT WRITTEN REQUEST.—No assessment may be required under paragraph (1) for a drug subject to an approved application under section 505 unless—

[(i) the Secretary has issued a written request for a related pediatric study under section 505A(c) of this Act or section 409I of the Public Health Service Act (42 U.S.C. 284m);

[(ii)(I) if the request was made under section 505A(c)—

[(aa) the recipient of the written request does not agree to the request; or

[(bb) the Secretary does not receive a response as specified under section 505A(d)(4)(A); or

[(II) if the request was made under section 409I of the Public Health Service Act (42 U.S.C. 284m)—

[(aa) the recipient of the written request does not agree to the request; or

[(bb) the Secretary does not receive a response as specified under section 409I(c)(2) of that Act; and

[(iii)(I) the Secretary certifies under subparagraph (B) that there are insufficient funds under sections 409I and 499 of the Public Health Service Act (42 U.S.C. 284m, 290b) to conduct the study; or

[(II) the Secretary publishes in the Federal Register a certification that certifies that—

[(aa) no contract or grant has been awarded under section 409I or 499 of the Public Health Service Act (42 U.S.C. 284m, 290b); and

[(bb) not less than 270 days have passed since the date of a certification under subparagraph (B) that there are sufficient funds to conduct the study.

[(B) NO AGREEMENT TO REQUEST.—Not later than 60 days after determining that no holder will agree to the written request (including a determination that the Secretary has not received a response specified under section 505A(d) of this Act or section 409I of the Public Health Service Act (42 U.S.C. 284m), the Secretary shall certify whether the Secretary has sufficient funds to conduct the study under section 409I or 499 of the Public Health Service Act (42 U.S.C. 284m, 290b), taking into account the prioritization under section 409I.

[(c) MEANINGFUL THERAPEUTIC BENEFIT.—For the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I) of subsection (a) and paragraphs (1)(B)(i) and (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological product shall be considered to represent a meaningful therapeutic benefit over existing therapies if the Secretary estimates that—

[(1) if approved, the drug or biological product would represent a significant improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or

[(2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options.

[(d) SUBMISSION OF ASSESSMENTS.—If a person fails to submit an assessment described in subsection (a)(2), or a request for approval of a pediatric formulation described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b)—

[(1) the drug or biological product that is the subject of the assessment or request may be considered misbranded solely because of that failure and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 303); but

[(2) the failure to submit the assessment or request shall not be the basis for a proceeding—

[(A) to withdraw approval for a drug under section 505(e); or

[(B) to revoke the license for a biological product under section 351 of the Public Health Service Act (42 U.S.C. 262).

[(e) MEETINGS.—Before and during the investigational process for a new drug or biological product, the Secretary shall meet at appropriate times with the sponsor of the new drug or biological product to discuss—

[(1) information that the sponsor submits on plans and timelines for pediatric studies; or

[(2) any planned request by the sponsor for waiver or deferral of pediatric studies.

[(f) SCOPE OF AUTHORITY.—Nothing in this section provides to the Secretary any authority to require a pediatric assessment of any drug or biological product, or any assessment regarding other populations or uses of a drug or biological product, other than the pediatric assessments described in this section.

[(g) ORPHAN DRUGS.—Unless the Secretary requires otherwise by regulation, this section does not apply to any drug for an indication for which orphan designation has been granted under section 526.

[(h) INTEGRATION WITH OTHER PEDIATRIC STUDIES.—The authority under this section shall remain in effect so long as an application subject to this section may be accepted for filing by the Secretary on or before the date specified in section 505A(n).]

SEC. 505A. PEDIATRIC STUDIES OF DRUGS.

(a) DEFINITIONS.—As used in this section, the term "pediatric studies" or "studies" means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups (including neonates in appropriate cases) in which a drug is anticipated to be used, and at the discretion of the Secretary, may include preclinical studies.

(b) MARKET EXCLUSIVITY FOR NEW DRUGS.—

(1) IN GENERAL.—Except as provided in paragraph (2), if, prior to approval of an application that is submitted under section 505(b)(1), the Secretary determines that information relat-

ing to the use of a new drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with subsection (d)(3), and if the Secretary has determined that labeling changes are appropriate, such changes are approved within the timeframe requested by the Secretary—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 505, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(E) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(2) EXCEPTION.—The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination is made later than one year prior to the expiration of such period.

(c) MARKET EXCLUSIVITY FOR ALREADY-MARKETED DRUGS.—

(1) IN GENERAL.—Except as provided in paragraph (2), if the Secretary determines that information relating to the use of an approved drug in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under section 505(b)(1) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe and the reports thereof are submitted and accepted in accordance with subsection (d)(3), and if the Secretary determines that labeling changes are appropriate and such changes are approved within the timeframe requested by the Secretary—

(A)(i)(I) the period referred to in subsection (c)(3)(E)(ii) of section 505, and in subsection (j)(5)(F)(ii) of such section, is deemed to be five years and six months rather than five years, and the references in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of such section to four years, to forty-eight months, and to seven and one-half years are deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(II) the period referred to in clauses (iii) and (iv) of subsection (c)(3)(D) of such section, and in clauses (iii) and (iv) of subsection (j)(5)(F) of such section, is deemed to be three years and six months rather than three years; and

(ii) if the drug is designated under section 526 for a rare disease or condition, the period referred to in section 527(a) is deemed to be seven years and six months rather than seven years; and

(B)(i) if the drug is the subject of—

(I) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(II) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B)(ii) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(ii) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(5)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions)

(2) EXCEPTION.—The Secretary shall not extend the period referred to in paragraph (1)(A) or (1)(B) if the determination is made later than one year prior to the expiration of such period.

(d) CONDUCT OF PEDIATRIC STUDIES.—

(1) REQUEST FOR STUDIES.—

(A) IN GENERAL.—The Secretary may, after consultation with the sponsor of an application for an investigational new drug under section 505(i), the sponsor of an application for a new drug under section 505(b)(1), or the holder of an approved application for a drug under section 505(b)(1) issue to the sponsor or holder a written request for the conduct of pediatric studies for such drug. In issuing such request, the Secretary shall take into account adequate representation of children of ethnic and racial minorities. Such request to conduct pediatric studies shall be in writing and shall include a timeframe for such studies and a request to the sponsor or holder to propose pediatric labeling resulting from such studies.

(B) SINGLE WRITTEN REQUEST.—A single written request—

(i) may relate to more than one use of a drug; and

(ii) may include uses that are both approved and unapproved.

(2) WRITTEN REQUEST FOR PEDIATRIC STUDIES.—

(A) REQUEST AND RESPONSE.—

(i) IN GENERAL.—If the Secretary makes a written request for pediatric studies (including neonates, as appropriate) under subsection (b) or (c), the applicant or holder, not later than 180 days after receiving the written request, shall respond to the Secretary as to the intention of the applicant or holder to act on the request by—

(I) indicating when the pediatric studies will be initiated, if the applicant or holder agrees to the request; or

(II) indicating that the applicant or holder does not agree to the request and stating the reasons for declining the request.

(ii) DISAGREE WITH REQUEST.—If, on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the applicant or holder does not agree to the request on the grounds that it is not possible to develop the appropriate pediatric formulation, the applicant or holder shall submit to the Secretary the reasons such pediatric formulation cannot be developed.

(B) ADVERSE EVENT REPORTS.—An applicant or holder that, on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, agrees to the request for such studies shall provide the Secretary, at the same time as the submission of the reports of such studies, with all postmarket adverse event reports regarding the drug that is the subject of such studies and are available prior to submission of such reports.

(3) MEETING THE STUDIES REQUIREMENT.—Not later than 180 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or

rejecting the reports shall be to determine, within the 180-day period, whether the studies fairly respond to the written request, have been conducted in accordance with commonly accepted scientific principles and protocols, and have been reported in accordance with the requirements of the Secretary for filing.

(4) EFFECT OF SUBSECTION.—Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(e) NOTICE OF DETERMINATIONS ON STUDIES REQUIREMENT.—

(1) IN GENERAL.—The Secretary shall publish a notice of any determination, made on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, that the requirements of subsection (d) have been met and that submissions and approvals under subsection (b)(2) or (j) of section 505 for a drug will be subject to the provisions of this section. Such notice shall be published not later than 30 days after the date of the Secretary's determination regarding market exclusivity and shall include a copy of the written request made under subsection (b) or (c).

(2) IDENTIFICATION OF CERTAIN DRUGS.—The Secretary shall publish a notice identifying any drug for which, on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, a pediatric formulation was developed, studied, and found to be safe and effective in the pediatric population (or specified subpopulation) if the pediatric formulation for such drug is not introduced onto the market within one year after the date that the Secretary publishes the notice described in paragraph (1). Such notice identifying such drug shall be published not later than 30 days after the date of the expiration of such one year period.

(f) INTERNAL REVIEW OF WRITTEN REQUESTS AND PEDIATRIC STUDIES.—

(1) INTERNAL REVIEW.—

(A) IN GENERAL.—The Secretary shall establish an internal review committee to review all written requests issued on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, in accordance with paragraph (2).

(B) MEMBERS.—The committee established under subparagraph (A) shall include individuals with expertise in pediatrics, biopharmacology, statistics, drugs and drug formulations, legal issues, pediatric ethics, the appropriate expertise, such as expertise in child and adolescent psychiatry, pertaining to the pediatric product under review, one or more experts from the Office of Pediatric Therapeutics, and other individuals designated by the Secretary.

(2) REVIEW OF WRITTEN REQUESTS.—The committee established under paragraph (1) shall review all written requests issued pursuant to this section prior to being issued.

(3) TRACKING PEDIATRIC STUDIES AND LABELING CHANGES.—The Secretary shall track and make available to the public, in an easily accessible manner, including through posting on the website of the Food and Drug Administration—

(A) the number of studies conducted under this section and under section 409I of the Public Health Service Act;

(B) the specific drugs and biological products and their uses, including labeled and off-labeled indications, studied under such sections;

(C) the types of studies conducted under such sections, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons such formulations were not developed;

(E) the labeling changes made as a result of studies conducted under such sections;

(F) an annual summary of labeling changes made as a result of studies conducted under such sections for distribution pursuant to subsection (k)(2); and

(G) information regarding reports submitted on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007.

(4) COMMITTEE.—The committee established under paragraph (1) shall be the committee utilized under section 505B(f)(1).

(g) LIMITATIONS.—Notwithstanding subsection (c)(2), a drug to which the six-month period under subsection (b) or (c) has already been applied—

(1) may receive an additional six-month period under subsection (c)(1)(A)(i)(II) for a supplemental application if all other requirements under this section are satisfied; and

(2) may not receive any additional such period under subsection (c)(1)(A)(ii).

(h) RELATIONSHIP TO PEDIATRIC RESEARCH REQUIREMENTS.—Notwithstanding any other provision of law, if any pediatric study is required by a provision of law (including a regulation) other than this section and such study meets the completeness, timeliness, and other requirements of this section, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.

(i) LABELING CHANGES.—

(1) PRIORITY STATUS FOR PEDIATRIC APPLICATIONS AND SUPPLEMENTS.—Any application or supplement to an application under section 505 proposing a labeling change as a result of any pediatric study conducted pursuant to this section—

(A) shall be considered to be a priority application or supplement; and

(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

(2) DISPUTE RESOLUTION.—

(A) REQUEST FOR LABELING CHANGE AND FAILURE TO AGREE.—If, on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the Commissioner determines that the sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application, not later than 180 days after the date of submission of the application—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor of the application does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) CONSIDERATION OF RECOMMENDATIONS.—The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling change that the Commissioner determines to be appropriate.

(D) MISBRANDING.—If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded.

(E) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under this Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(j) OTHER LABELING CHANGES.—If, on or after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary determines that a pediatric study conducted under this section does or does not demonstrate that the drug that is the subject of the study is safe and effective in pediatric populations or subpopulations, including whether such study results are inconclusive, the Secretary shall order the labeling of such product to include information about the results of the study and a statement of the Secretary's determination.

(k) DISSEMINATION OF PEDIATRIC INFORMATION.—

(1) IN GENERAL.—Not later than 180 days after the date of submission of a report on a pediatric study under this section, the Secretary shall make available to the public the medical, statistical, and clinical pharmacology reviews of pediatric studies conducted under subsection (b) or (c).

(2) DISSEMINATION OF INFORMATION REGARDING LABELING CHANGES.—Beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary shall include as a requirement of a written request that the sponsors of the studies that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(3)(F) distribute, at least annually (or more frequently if the Secretary determines that it would be beneficial to the public

health), such information to physicians and other health care providers.

(3) EFFECT OF SUBSECTION.—Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(l) ADVERSE EVENT REPORTING.—

(1) REPORTING IN YEAR ONE.—Beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, during the one-year period beginning on the date a labeling change is approved pursuant to subsection (i), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics established under section 6 of the Best Pharmaceuticals for Children Act (Public Law 107–109). In considering the reports, the Director of such Office shall provide for the review of the reports by the Pediatric Advisory Committee, including obtaining any recommendations of such Committee regarding whether the Secretary should take action under this Act in response to such reports.

(2) REPORTING IN SUBSEQUENT YEARS.—Following the one-year period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering such reports, the Director of such Office may provide for the review of such reports by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such reports.

(3) EFFECT.—The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(m) CLARIFICATION OF INTERACTION OF MARKET EXCLUSIVITY UNDER THIS SECTION AND MARKET EXCLUSIVITY AWARDED TO AN APPLICANT FOR APPROVAL OF A DRUG UNDER SECTION 505(j).—If a 180-day period under section 505(j)(5)(B)(iv) overlaps with a 6-month exclusivity period under this section, so that the applicant for approval of a drug under section 505(j) entitled to the 180-day period under that section loses a portion of the 180-day period to which the applicant is entitled for the drug, the 180-day period shall be extended from—

(1) the date on which the 180-day period would have expired by the number of days of the overlap, if the 180-day period would, but for the application of this subsection, expire after the 6-month exclusivity period; or

(2) the date on which the 6-month exclusivity period expires, by the number of days of the overlap if the 180-day period would, but for the application of this subsection, expire during the six-month exclusivity period.

(n) REFERRAL IF PEDIATRIC STUDIES NOT COMPLETED.—

(1) IN GENERAL.—Beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, if pediatric studies have not been completed under subsection (d) and if the Secretary, through the committee established under subsection

(f), determines that there is a continuing need for information relating to the use of the drug in the pediatric population (including neonates, as appropriate), the Secretary shall—

(A) for a drug for which listed patents have not expired, make a determination regarding whether an assessment shall be required to be submitted under section 505B; or

(B) for a drug that has no listed patents or has 1 or more listed patents that have expired, determine whether there are funds available under section 736 to award a grant to conduct the requested studies pursuant to paragraph (2).

(2) FUNDING OF STUDIES.—If, pursuant to paragraph (1), the Secretary determines that there are funds available under section 736 to award a grant to conduct the requested pediatric studies, then the Secretary shall issue a proposal to award a grant to conduct the requested studies. If the Secretary determines that funds are not available under section 736, the Secretary shall refer the drug for inclusion on the list established under section 409I of the Public Health Service Act or the conduct of studies.

(3) PUBLIC NOTICE.—The Secretary shall give the public notice of—

(A) a decision under paragraph (1)(A) not to require an assessment under section 505B and the basis for such decision;

(B) the name of any drug, its manufacturer, and the indications to be studied pursuant to a grant made under paragraph (2); and

(C) any decision under paragraph (2) to include a drug on the list established under section 409I of the Public Health Service Act.

(4) EFFECT OF SUBSECTION.—Nothing in this subsection alters or amends section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(o) PROMPT APPROVAL OF DRUGS UNDER SECTION 505(j) WHEN PEDIATRIC INFORMATION IS ADDED TO LABELING.—

(1) GENERAL RULE.—A drug for which an application has been submitted or approved under section 505(j) shall not be considered ineligible for approval under that section or misbranded under section 502 on the basis that the labeling of the drug omits a pediatric indication or any other aspect of labeling pertaining to pediatric use when the omitted indication or other aspect is protected by patent or by exclusivity under clause (iii) or (iv) of section 505(j)(5)(F).

(2) LABELING.—Notwithstanding clauses (iii) and (iv) of section 505(j)(5)(F), the Secretary may require that the labeling of a drug approved under section 505(j) that omits a pediatric indication or other aspect of labeling as described in paragraph (1) include—

(A) a statement that, because of marketing exclusivity for a manufacturer—

(i) the drug is not labeled for pediatric use; or

(ii) in the case of a drug for which there is an additional pediatric use not referred to in paragraph (1), the drug is not labeled for the pediatric use under paragraph (1); and

(B) a statement of any appropriate pediatric contraindications, warnings, or precautions that the Secretary considers necessary.

(3) PRESERVATION OF PEDIATRIC EXCLUSIVITY AND OTHER PROVISIONS.—This subsection does not affect—

(A) the availability or scope of exclusivity under this section;

(B) the availability or scope of exclusivity under section 505 for pediatric formulations;

(C) the question of the eligibility for approval of any application under section 505(j) that omits any other conditions of approval entitled to exclusivity under clause (iii) or (iv) of section 505(j)(5)(F); or

(D) except as expressly provided in paragraphs (1) and (2), the operation of section 505.

(p) INSTITUTE OF MEDICINE STUDY.—Not later than 3 years after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary shall enter into a contract with the Institute of Medicine to conduct a study and report to Congress regarding the written requests made and the studies conducted pursuant to this section. The Institute of Medicine may devise an appropriate mechanism to review a representative sample of requests made and studies conducted pursuant to this section in order to conduct such study. Such study shall—

(1) review such representative written requests issued by the Secretary since 1997 under subsections (b) and (c);

(2) review and assess such representative pediatric studies conducted under subsections (b) and (c) since 1997 and labeling changes made as a result of such studies;

(3) review the use of extrapolation for pediatric subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, and ethical issues in pediatric clinical trials; and

(4) make recommendations regarding appropriate incentives for encouraging pediatric studies of biologics.

(q) SUNSET.—A drug may not receive any 6-month period under subsection (b) or (c) unless—

(1) on or before October 1, 2012, the Secretary makes a written request for pediatric studies of the drug;

(2) on or before October 1, 2012, an application for the drug is accepted for filing under section 505(b); and

(3) all requirements of this section are met.

SEC. 505B. RESEARCH INTO PEDIATRIC USES FOR DRUGS AND BIOLOGICAL PRODUCTS.

(a) NEW DRUGS AND BIOLOGICAL PRODUCTS.—

(1) IN GENERAL.—A person that submits, on or after the date of enactment of the Pediatric Research Equity Act of 2007, an application (or supplement to an application)—

(A) under section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration, or

(B) under section 351 of the Public Health Service Act (42 U.S.C. 262) for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration,

shall submit with the application the assessments described in paragraph (2).

(2) ASSESSMENTS.—

(A) IN GENERAL.—The assessments referred to in paragraph (1) shall contain data, gathered using appropriate formulations for each age group for which the assessment is required, that are adequate—

(i) to assess the safety and effectiveness of the drug or the biological product for the claimed indications in all relevant pediatric subpopulations; and

(ii) to support dosing and administration for each pediatric subpopulation for which the drug or the biological product is safe and effective.

(B) SIMILAR COURSE OF DISEASE OR SIMILAR EFFECT OF DRUG OR BIOLOGICAL PRODUCT.—

(i) IN GENERAL.—If the course of the disease and the effects of the drug are sufficiently similar in adults and pediatric patients, the Secretary may conclude that pediatric effectiveness can be extrapolated from adequate and well-controlled studies in adults, usually supplemented with other information obtained in pediatric patients, such as pharmacokinetic studies.

(ii) EXTRAPOLATION BETWEEN AGE GROUPS.—A study may not be needed in each pediatric age group if data from one age group can be extrapolated to another age group.

(iii) INFORMATION ON EXTRAPOLATION.—A brief documentation of the scientific data supporting the conclusion under clauses (i) and (ii) shall be included in the medical review that is collected as part of the application under section 505 of this Act or section 351 of the Public Health Service Act (42 U.S.C. 262).

(3) DEFERRAL.—

(A) IN GENERAL.—On the initiative of the Secretary or at the request of the applicant, the Secretary may defer submission of some or all assessments required under paragraph (1) until a specified date after approval of the drug or issuance of the license for a biological product if—

(i) the Secretary finds that—

(I) the drug or biological product is ready for approval for use in adults before pediatric studies are complete;

(II) pediatric studies should be delayed until additional safety or effectiveness data have been collected; or

(III) there is another appropriate reason for deferral; and

(ii) the applicant submits to the Secretary—

(I) certification of the grounds for deferring the assessments;

(II) a description of the planned or ongoing studies;

(III) evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time; and

(IV) a timeline for the completion of such studies.

(B) ANNUAL REVIEW.—

(i) IN GENERAL.—On an annual basis following the approval of a deferral under subparagraph (A), the applicant shall submit to the Secretary the following information:

(I) Information detailing the progress made in conducting pediatric studies.

(II) If no progress has been made in conducting such studies, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time.

(ii) PUBLIC AVAILABILITY.—The information submitted through the annual review under clause (i) shall promptly be made available to the public in an easily accessible manner, including through the website of the Food and Drug Administration.

(4) WAIVERS.—

(A) FULL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients is so small or the patients are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups; or

(iii) The drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(II) is not likely to be used in a substantial number of pediatric patients.

(B) PARTIAL WAIVER.—On the initiative of the Secretary or at the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments for a drug or biological product under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii) the drug or biological product—

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(II) is not likely to be used by a substantial number of pediatric patients in that age group; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the website of the Food and Drug Administration.

(D) LABELING REQUIREMENT.—If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

(b) MARKETED DRUGS AND BIOLOGICAL PRODUCTS.—

(1) IN GENERAL.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, after providing notice in the form of a letter and an opportunity for written response and a meeting, which may include an advisory committee meeting, the Secretary may (by order in the form of a letter) require the sponsor or holder of an approved application for a drug under section 505 or the holder of a license for a biological product under section 351 of the Public Health Service Act to submit by a specified date the assessments described in subsection (a)(2), if the Secretary finds that—

(A)(i) the drug or biological product is used for a substantial number of pediatric patients for the labeled indications; and

(ii) adequate pediatric labeling could confer a benefit on pediatric patients;

(B) there is reason to believe that the drug or biological product would represent a meaningful therapeutic benefit over existing therapies for pediatric patients for 1 or more of the claimed indications; or

(C) the absence of adequate pediatric labeling could pose a risk to pediatric patients.

(2) WAIVERS.—

(A) FULL WAIVER.—At the request of an applicant, the Secretary shall grant a full waiver, as appropriate, of the requirement to submit assessments under this subsection if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed); or

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in all pediatric age groups.

(B) PARTIAL WAIVER.—At the request of an applicant, the Secretary shall grant a partial waiver, as appropriate, of the requirement to submit assessments under this subsection with respect to a specific pediatric age group if the applicant certifies and the Secretary finds that—

(i) necessary studies are impossible or highly impracticable (because, for example, the number of patients in that age group is so small or patients in that age group are geographically dispersed);

(ii) there is evidence strongly suggesting that the drug or biological product would be ineffective or unsafe in that age group;

(iii)(I) the drug or biological product—

(aa) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in that age group; and

(bb) is not likely to be used in a substantial number of pediatric patients in that age group; and

(II) the absence of adequate labeling could not pose significant risks to pediatric patients; or

(iv) the applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for that age group have failed.

(C) PEDIATRIC FORMULATION NOT POSSIBLE.—If a waiver is granted on the ground that it is not possible to develop a pediatric formulation, the waiver shall cover only the pediatric groups requiring that formulation. An applicant seeking either a full or partial waiver shall submit to the Secretary documentation detailing why a pediatric formulation cannot be developed and, if the waiver is granted, the applicant's submission shall promptly be made available to the public in an easily accessible manner, including through posting on the website of the Food and Drug Administration.

(D) LABELING REQUIREMENT.—If the Secretary grants a full or partial waiver because there is evidence that a drug or biological product would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug or biological product.

(c) MEANINGFUL THERAPEUTIC BENEFIT.—For the purposes of paragraph (4)(A)(iii)(I) and (4)(B)(iii)(I) of subsection (a) and paragraphs (1)(B)(I) and (2)(B)(iii)(I)(aa) of subsection (b), a drug or biological product shall be considered to represent a meaningful therapeutic benefit over existing therapies if the Secretary determines that—

(1) if approved, the drug or biological product could represent an improvement in the treatment, diagnosis, or prevention of a disease, compared with marketed products adequately labeled for that use in the relevant pediatric population; or

(2) the drug or biological product is in a class of products or for an indication for which there is a need for additional options.

(d) SUBMISSION OF ASSESSMENTS.—If a person fails to submit an assessment described in subsection (a)(2), or a request for approval

of a pediatric formulation described in subsection (a) or (b), in accordance with applicable provisions of subsections (a) and (b)—

(1) the drug or biological product that is the subject of the assessment or request may be considered misbranded solely because of that failure and subject to relevant enforcement action (except that the drug or biological product shall not be subject to action under section 303); but

(2) the failure to submit the assessment or request shall not be the basis for a proceeding—

(A) to withdraw approval for a drug under section 505(e); or

(B) to revoke the license for a biological product under section 351 of the Public Health Service Act.

(e) MEETINGS.—Before and during the investigational process for a new drug or biological product, the Secretary shall meet at appropriate times with the sponsor of the new drug or biological product to discuss—

(1) information that the sponsor submits on plans and timelines for pediatric studies; or

(2) any planned request by the sponsor for waiver or deferral of pediatric studies.

(f) REVIEW OF PEDIATRIC PLANS, DEFERRALS, AND WAIVERS.—

(1) REVIEW.—Beginning not later than 30 days after the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall utilize an internal committee to provide consultation to reviewing divisions on all pediatric plans and assessments prior to approval of an application or supplement for which a pediatric assessment is required under this section and all deferral and waiver requests granted pursuant to this section. Such internal committee shall include employees of the Food and Drug Administration, with expertise in pediatrics (including representation from the Office of Pediatric Therapeutics), biopharmacology, statistics, chemistry, legal issues, pediatric ethics, and the appropriate expertise pertaining to the pediatric product under review, and other individuals designated by the Secretary.

(2) ACTIVITY BY COMMITTEE.—The committee referred to in paragraph (1) may operate using appropriate members of such committee and need not convene all members of the committee.

(3) DOCUMENTATION OF COMMITTEE ACTION.—For each drug or biological product, the committee referred to in paragraph (1) shall document, for each activity described in paragraph (4), which members of the committee participated in such activity.

(4) REVIEW OF PEDIATRIC PLANS, DEFERRALS AND WAIVERS.—Consultation on pediatric plans and assessments by the internal committee pursuant to this section shall occur prior to approval of an application or supplement for which a pediatric assessment is required under this section. The internal committee shall review all requests for deferrals and waivers from the requirement to submit a pediatric assessment granted under this section and shall provide recommendations as needed to reviewing divisions.

(5) RETROSPECTIVE REVIEW OF PEDIATRIC PLANS, DEFERRALS AND WAIVERS.—Within one year after enactment of the Pediatric Research Equity Act of 2007, the committee shall conduct a ret-

rospective review and analysis of a representative sample of assessments submitted and deferrals and waivers approved under this section since enactment of the Pediatric Research Equity Act of 2003. Such review shall include an analysis of the quality and consistency of pediatric information in pediatric assessments and the appropriateness of waivers and deferrals granted. Based on such review, the Secretary shall issue recommendations to the review divisions for improvements and initiate guidance to industry related to the scope of pediatric studies required under this section.

(6) TRACKING OF ASSESSMENTS AND LABELING CHANGES.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall track and make available to the public in an easily accessible manner, including through posting on the website of the Food and Drug Administration—

(A) the number of assessments conducted under this section;

(B) the specific drugs and biological products and their uses assessed under this section;

(C) the types of assessments conducted under this section, including trial design, the number of pediatric patients studied, and the number of centers and countries involved;

(D) the total number of deferrals requested and granted under this section and, if granted, the reasons for such deferrals, the timeline for completion, and the number completed and pending by the specified date, as outlined in subsection (a)(3);

(E) the number of waivers requested and granted under this section and, if granted, the reasons for the waivers;

(F) the number of pediatric formulations developed and the number of pediatric formulations not developed and the reasons any such formulation was not developed;

(G) the labeling changes made as a result of assessments conducted under this section;

(H) an annual summary of labeling changes made as a result of assessments conducted under this section for distribution pursuant to subsection (h)(2); and

(I) an annual summary of information submitted pursuant to subsection (a)(3)(B).

(7) COMMITTEE.—The committee utilized under paragraph (1) shall be the committee established under section 505A(f)(1).

(g) LABELING CHANGES.—

(1) PRIORITY STATUS FOR PEDIATRIC APPLICATIONS.—Any supplement to an application under section 505 and section 351 of the Public Health Service Act proposing a labeling change as a result of any pediatric assessments conducted pursuant to this section—

(A) shall be considered a priority application or supplement; and

(B) shall be subject to the performance goals established by the Commissioner for priority drugs.

(2) DISPUTE RESOLUTION.—

(A) REQUEST FOR LABELING CHANGE AND FAILURE TO AGREE.—If, on or after the date of enactment of the Pediatric Research Equity Act of 2007, the Commissioner deter-

mines that a sponsor and the Commissioner have been unable to reach agreement on appropriate changes to the labeling for the drug that is the subject of the application or supplement, not later than 180 days after the date of the submission of the application or supplement—

(i) the Commissioner shall request that the sponsor of the application make any labeling change that the Commissioner determines to be appropriate; and

(ii) if the sponsor does not agree within 30 days after the Commissioner's request to make a labeling change requested by the Commissioner, the Commissioner shall refer the matter to the Pediatric Advisory Committee.

(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A)(ii), the Pediatric Advisory Committee shall—

(i) review the pediatric study reports; and

(ii) make a recommendation to the Commissioner concerning appropriate labeling changes, if any.

(C) CONSIDERATION OF RECOMMENDATIONS.—The Commissioner shall consider the recommendations of the Pediatric Advisory Committee and, if appropriate, not later than 30 days after receiving the recommendation, make a request to the sponsor of the application to make any labeling changes that the Commissioner determines to be appropriate.

(D) MISBRANDING.—If the sponsor of the application, within 30 days after receiving a request under subparagraph (C), does not agree to make a labeling change requested by the Commissioner, the Commissioner may deem the drug that is the subject of the application to be misbranded.

(E) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under this Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(3) OTHER LABELING CHANGES.—If, on or after the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary makes a determination that a pediatric assessment conducted under this section does or does not demonstrate that the drug that is the subject of such assessment is safe and effective in pediatric populations or subpopulations, including whether such assessment results are inconclusive, the Secretary shall order the label of such product to include information about the results of the assessment and a statement of the Secretary's determination.

(h) DISSEMINATION OF PEDIATRIC INFORMATION.—

(1) IN GENERAL.—Not later than 180 days after the date of submission of a pediatric assessment under this section, the Secretary shall make available to the public in an easily accessible manner the medical, statistical, and clinical pharmacology

reviews of such pediatric assessments, and shall post such assessments on the website of the Food and Drug Administration.

(2) DISSEMINATION OF INFORMATION REGARDING LABELING CHANGES.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, the Secretary shall require that the sponsors of the assessments that result in labeling changes that are reflected in the annual summary developed pursuant to subsection (f)(6)(H) distribute such information to physicians and other health care providers.

(3) EFFECT OF SUBSECTION.—Nothing in this subsection shall alter or amend Section 301(j) of this Act or section 552 of title 5 or section 1905 of title 18, United States Code.

(i) ADVERSE EVENT REPORTING.—

(1) REPORTING IN YEAR ONE.—Beginning on the date of enactment of the Pediatric Research Equity Act of 2007, during the one-year period beginning on the date a labeling change is made pursuant to subsection (g), the Secretary shall ensure that all adverse event reports that have been received for such drug (regardless of when such report was received) are referred to the Office of Pediatric Therapeutics. In considering the report, the Director of such Office shall provide for the review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this Act in response to such report.

(2) REPORTING IN SUBSEQUENT YEARS.—Following the one-year period described in paragraph (1), the Secretary shall, as appropriate, refer to the Office of Pediatric Therapeutics all pediatric adverse event reports for a drug for which a pediatric study was conducted under this section. In considering the report, the Director of such Office may provide for the review of the report by the Pediatric Advisory Committee, including obtaining any recommendation of such Committee regarding whether the Secretary should take action in response to such report.

(3) EFFECT.—The requirements of this subsection shall supplement, not supplant, other review of such adverse event reports by the Secretary.

(j) SCOPE OF AUTHORITY.—Nothing in this section provides to the Secretary any authority to require a pediatric assessment of any drug or biological product, or any assessment regarding other populations or uses of a drug or biological product, other than the pediatric assessments described in this section.

(k) ORPHAN DRUGS.—Unless the Secretary requires otherwise by regulation, this section does not apply to any drug for an indication for which orphan designation has been granted under section 526.

(l) INSTITUTE OF MEDICINE STUDY.—

(1) IN GENERAL.—Not later than three years after the date of the enactment of the Pediatric Research Equity Act of 2007, the Secretary shall contract with the Institute of Medicine to conduct a study and report to Congress regarding the pediatric studies conducted pursuant to this section since 1997 and labeling changes made as a result of such studies.

(2) CONTENT OF STUDY.—The study under paragraph (1) shall review and assess the use of extrapolation for pediatric

subpopulations, the use of alternative endpoints for pediatric populations, neonatal assessment tools, the number and type of pediatric adverse events, and ethical issues in pediatric clinical trials.

(3) REPRESENTATIVE SAMPLE.—The Institute of Medicine may devise an appropriate mechanism to review a representative sample of studies conducted pursuant to this section from each review division within the Center for Drug Evaluation and Research in order to make the requested assessment.

SEC. 505C. PHARMACEUTICAL SECURITY.

(a) IN GENERAL.—The Secretary shall develop standards and identify and validate effective technologies for the purpose of securing the prescription drug distribution system against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

(b) STANDARDS DEVELOPMENT.—

(1) IN GENERAL.—The Secretary shall, in consultation with the agencies specified in paragraph (3), prioritize and develop standards for the identification, validation, authentication, and tracking of prescription drugs.

(2) PROMISING TECHNOLOGIES.—The standards developed under this subsection shall address promising technologies, including—

(A) radio frequency identification technology;

(B) nanotechnology;

(C) encryption technologies; and

(D) other track-and-trace technologies.

(3) INTERAGENCY COLLABORATION.—In carrying out this subsection, the Secretary shall consult with Federal health and security agencies, including—

(A) the Administrator of the Drug Enforcement Administration;

(B) the Secretary of the Department of Homeland Security

(C) the Secretary of Commerce; and

(D) other appropriate Federal and State agencies.

(c) INSPECTION AND ENFORCEMENT.—

(1) IN GENERAL.—The Secretary shall expand and enhance the resources and facilities of the Office of Regulatory Affairs of the Food and Drug Administration to protect the prescription drug distribution system against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

(2) ACTIVITIES.—The Secretary shall undertake enhanced and joint enforcement activities with other Federal agencies and State officials, and establish regional capacities for the validation of prescription drugs and the inspection of the prescription drug distribution system.

(d) DEFINITION.—In this section, the term "prescription drug" means a drug subject to section 503(b)(1).

* * * * * * *

REGISTRATION OF PRODUCERS OF DRUGS AND DEVICES

SEC. 510. (a) * * *

(b) [On or before] *(1) On or before* December 31 of each year every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs [or a device or devices] shall register with the Secretary his name, places of business, and all such establishments.

(2) During the period beginning on October 1 and ending on December 31 of each year, every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a device or devices shall register with the Secretary his name, places of business, and all such establishments.

* * * * * * *

(i)(1) [On or before December 31 of each year, any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or a device that is imported or offered for import into the United States shall, through electronic means in accordance with the criteria of the Secretary, register with the Secretary the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such drug or device in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug or device to the United States for purposes of importation.] *Any establishment within any foreign country engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device that is imported or offered for import into the United States shall, through electronic means in accordance with the criteria of the Secretary—*

(A) upon first engaging in any such activity, immediately register with the Secretary the name and place of business of the establishment, the name of the United States agent for the establishment, the name of each importer of such drug or device in the United States that is known to the establishment, and the name of each person who imports or offers for import such drug or device to the United States for purposes of importation; and

(B) each establishment subject to the requirements of subparagraph (A) shall thereafter—

(i) with respect to drugs, register with the Secretary on or before December 31 of each year; and

(ii) with respect to devices, register with the Secretary during the period beginning on October 1 and ending on December 31 of each year.

* * * * * * *

(j)(1) * * *

(2) [Each person who registers with the Secretary under this section shall report to the Secretary once during the month of June of each year and once during the month of December of each year the following information:] *Each person who registers with the Secretary under this section shall report to the Secretary, with regard to drugs once during the month of June of each year and once during the month of December of each year, and with regard to devices*

once each year during the period beginning on October 1 and ending on December 31, the following information:

(A) * * *

* * * * * * *

(k) Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use shall, at least ninety days before making such introduction or delivery, report to the Secretary or person who is accredited under section 523(a) (in such form and manner as the Secretary shall by regulation prescribe)—

(1) the class in which the device is classified under section 513 or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified, **[**and**]**

(2) action taken by such person to comply with requirements under section 514 or 515 which are applicable to the device**[**.**]**, *and*

(3) action taken by such person to comply with requirements under section 492C of the Public Health Service Act for the submission of clinical trial information for inclusion in the registry database and the results database described in such section.

* * * * * * *

[(p) Registrations under subsections (b), (c), (d), and (i) (including the submission of updated information) shall be submitted to the Secretary by electronic means, upon a finding by the Secretary that the electronic receipt of such registrations is feasible, unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver.**]**

(p)(1) Registrations and listings under this section (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver.

(2) With regard to any establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a device, the registration and listing information required by this section shall be submitted to the Secretary by electronic means, unless the Secretary grants a waiver because electronic registration and listing is not reasonable for the person requesting such waiver.

SEC. 511. CLINICAL TRIAL GUIDANCE FOR ANTIBIOTIC DRUGS.

(a) IN GENERAL.—Not later than 1 year after the date of enactment of this section, the Secretary, acting through the Commissioner of Food and Drugs, shall issue guidance for the conduct of clinical trials with respect to antibiotic drugs, including antimicrobials to treat acute bacterial sinusitis, acute bacterial otitis media, and acute bacterial exacerbation of chronic bronchitis. Such guidelines shall indicate the appropriate animal models of infection, in vitro techniques, and valid microbiologic surrogate markers.

(b) REVIEW.—Not later than 5 years after the date of enactment of this section, the Secretary, acting through the Commissioner of Food and Drugs, shall review and update the guidance described

under subsection (a) to reflect developments in scientific and medical information and technology.

* * * * * * *

PREMARKET APPROVAL

General Requirement

SEC. 515. (a) * * *

* * * * * * *

Action on an Application for Premarket Approval

(d)(1) * * *

(2) The Secretary shall deny approval of an application for a device if, upon the basis of the information submitted to the Secretary as part of the application and any other information before him with respect to such device, the Secretary finds that—

(A) * * *

* * * * * * *

(D) based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particular; **[**or**]**

(E) such device is not shown to conform in all respects to a performance standard in effect under section 514 compliance with which is a condition to approval of the application and there is a lack of adequate information to justify the deviation from such standard**[**.**]***; or*

(F) the applicant is in violation of the requirements under section 492C of the Public Health Service Act for the submission of clinical trial information for inclusion in the registry database or the results database described in such section.

* * * * * * *

SEC. 515A. PEDIATRIC USES OF DEVICES.

(a) NEW DEVICES.—

(1) IN GENERAL.—A person that submits to the Secretary an application under section 520(m), or an application (or supplement to an application) or a product development protocol under section 515, shall include in the application or protocol the information described in paragraph (2).

(2) REQUIRED INFORMATION.—The application or protocol described in paragraph (1) shall include, with respect to the device for which approval is sought and if readily available—

(A) a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure; and

(B) the number of affected pediatric patients.

(3) ANNUAL REPORT.—Not later than 18 months after the date of enactment of this section, and annually thereafter, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report that includes—

(A) the number of devices approved in the year preceding the year in which the report is submitted, for which there

is a pediatric subpopulation that suffers from the disease or condition that the device is intended to treat, diagnose, or cure;

(B) the number of devices approved in the year preceding the year in which the report is submitted, labeled for use in pediatric patients;

(C) the number of pediatric devices approved in the year preceding the year in which the report is submitted, exempted from a fee pursuant to section 738(a)(2)(B)(v); and

(D) the review time for each device described in subparagraphs (A), (B), and (C).

(b) DETERMINATION OF PEDIATRIC EFFECTIVENESS BASED ON SIMILAR COURSE OF DISEASE OR CONDITION OR SIMILAR EFFECT OF DEVICE ON ADULTS.—

(1) IN GENERAL.—If the course of the disease or condition and the effects of the device are sufficiently similar in adults and pediatric patients, the Secretary may conclude that adult data may be used to support a determination of a reasonable assurance of effectiveness in pediatric populations, as appropriate.

(2) EXTRAPOLATION BETWEEN SUBPOPULATIONS.—A study may not be needed in each pediatric subpopulation if data from one subpopulation can be extrapolated to another subpopulation.

(c) PEDIATRIC SUBPOPULATION.—For purposes of this section, the term "pediatric subpopulation" has the meaning given the term in section 520(m)(6)(E)(ii).

* * * * * * *

RECORDS AND REPORTS ON DEVICES

General Rule

SEC. 519. (a) Every person who is a manufacturer or importer of a device intended for human use shall establish and maintain such records, make such reports, and provide such information, as the Secretary may by regulation reasonably require to assure that such device is not adulterated or misbranded and to otherwise assure its safety and effectiveness. Regulations prescribed under the preceding sentence—

(1) * * *

(A) may have caused or contributed to a death or serious injury, or

(B) has malfunctioned and that such device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction [were to recur;] *were to recur, which report under this subparagraph—*

(i) shall be submitted in accordance with part 803 of title 21, Code of Federal Regulations (or successor regulations), if the device involved is—

(I) a class III device;

(II) a class II device that is permanently implantable, is life supporting, or is life sustaining; or

(III) a type of device that the Secretary has by regulation determined should be subject to such part 803 in order to protect the public health; or

(ii) shall, if the device is not subject to clause (i), be submitted in accordance with criteria established by the Secretary for reports made pursuant to this clause, which criteria shall require the reports to be in summary form and made on a quarterly basis;

* * * * * * *

Unique Device Identification System

(f) The Secretary shall promulgate regulations establishing a unique device identification system for medical devices requiring the labeling of devices to bear a unique identifier.

Reports of Removals and Corrections

[(f)**]** *(g)*(1) * * *

* * * * * * *

GENERAL PROVISIONS RESPECTING CONTROL OF DEVICES INTENDED FOR HUMAN USE

General Rule

SEC. 520. (a) * * *

* * * * * * *

Exemption for Devices for Investigational Use

(g)(1) * * *

(2)(A) * * *

(B) The conditions prescribed pursuant to subparagraph (A) shall include the following:

(i) * * *

* * * * * * *

(iii) A requirement that the person applying for an exemption for a device assure that such person is in compliance with the requirements of section 492C of the Public Health Service Act for the submission of clinical trial information for inclusion in the registry database and the results database described in such section.

[(iii)**]** *(iv)* Such other requirements as the Secretary may determine to be necessary for the protection of the public health and safety.

* * * * * * *

HUMANITARIAN DEVICE EXEMPTION

(m)(1) * * *

* * * * * * *

(3) **[**No**]** *Except as provided in paragraph (6), no* person granted an exemption under paragraph (2) with respect to a device may sell

the device for an amount that exceeds the costs of research and development, fabrication, and distribution of the device.

* * * * * * *

(5) The Secretary may require a person granted an exemption under paragraph (2) to demonstrate continued compliance with the requirements of this subsection if the Secretary believes such demonstration to be necessary to protect the public health*, if the Secretary has reason to believe that the requirements of paragraph (6) are no longer met,* or if the Secretary has reason to believe that the criteria for the exemption are no longer met. *If the person granted an exemption under paragraph (2) fails to demonstrate continued compliance with the requirements of this subsection, the Secretary may suspend or withdraw the exemption from the effectiveness requirements of sections 514 and 515 for a humanitarian device only after providing notice and an opportunity for an informal hearing.*

[(6) The Secretary may suspend or withdraw an exemption from the effectiveness requirements of sections 514 and 515 for a humanitarian device only after providing notice and an opportunity for an informal hearing.**]**

(6)(A) Except as provided in subparagraph (D), the prohibition in paragraph (3) shall not apply with respect to a person granted an exemption under paragraph (2) if each of the following conditions apply:

(i)(I) The device with respect to which the exemption is granted is intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs.

(II) The device was not previously approved under this subsection for the pediatric patients or the pediatric subpopulation described in subclause (I) prior to the date of enactment of the Pediatric Medical Device Safety and Improvement Act of 2007.

(ii) During any calendar year, the number of such devices distributed during that year does not exceed the annual distribution number specified by the Secretary when the Secretary grants such exemption. The annual distribution number shall be based on the number of individuals affected by the disease or condition that such device is intended to treat, diagnose, or cure, and of that number, the number of individuals likely to use the device, and the number of devices reasonably necessary to treat such individuals. In no case shall the annual distribution number exceed the number identified in paragraph (2)(A).

(iii) Such person immediately notifies the Secretary if the number of such devices distributed during any calendar year exceeds the annual distribution number referred to in clause (ii).

(iv) The request for such exemption is submitted on or before October 1, 2013.

(B) The Secretary may inspect the records relating to the number of devices distributed during any calendar year of a person granted an exemption under paragraph (2) for which the prohibition in paragraph (3) does not apply.

(C) A person may petition the Secretary to modify the annual distribution number specified by the Secretary under subparagraph

(A)(ii) with respect to a device if additional information on the number of individuals affected by the disease or condition arises, and the Secretary may modify such number but in no case shall the annual distribution number exceed the number identified in paragraph (2)(A).

(D) If a person notifies the Secretary, or the Secretary determines through an inspection under subparagraph (B), that the number of devices distributed during any calendar year exceeds the annual distribution number, as required under subparagraph (A)(iii), and modified under subparagraph (C), if applicable, then the prohibition in paragraph (3) shall apply with respect to such person for such device for any sales of such device after such notification.

(E)(i) In this subsection, the term "pediatric patients" means patients who are 21 years of age or younger at the time of the diagnosis or treatment.

(ii) In this subsection, the term "pediatric subpopulation" means 1 of the following populations:

(I) Neonates.

(II) Infants.

(III) Children.

(IV) Adolescents.

(7) The Secretary shall refer any report of an adverse event regarding a device for which the prohibition under paragraph (3) does not apply pursuant to paragraph (6)(A) that the Secretary receives to the Office of Pediatric Therapeutics, established under section 6 of the Best Pharmaceuticals for Children Act (Public Law 107–109. In considering the report, the Director of the Office of Pediatric Therapeutics, in consultation with experts in the Center for Devices and Radiological Health, shall provide for periodic review of the report by the Pediatric Advisory Committee, including obtaining any recommendations of such committee regarding whether the Secretary should take action under this Act in response to the report.

(8) In consultation with the Office of Pediatric Therapeutics and the Center for Devices and Radiological Health, the Secretary shall provide for an annual review by the Pediatric Advisory Committee of all devices described in paragraph (6) to ensure that the exemption under paragraph (2) remains appropriate for the pediatric populations for which it is granted.

* * * * * * *

POSTMARKET SURVEILLANCE

SEC. 522. (a) IN GENERAL.—The Secretary may by order, *or as a condition to approval of an application (or a supplement to an application) or a product development protocol under section 515 or as a condition to clearance of a premarket notification under section 510(k), for a pediatric population or pediatric subpopulation,* require a manufacturer to conduct postmarket surveillance for any device of the manufacturer which is a class II or class III device the failure of which would be reasonably likely to have serious adverse health consequences*, or that is indicated for pediatric populations or subpopulations or is expected to have significant use in pediatric populations,* or which is intended to be—

(1) * * *

* * * * * * *

[(b) SURVEILLANCE APPROVAL.—Each]

(b) SURVEILLANCE APPROVAL.—

(1) IN GENERAL.—Each manufacturer required to conduct a surveillance of a device shall, within 30 days of receiving an order from the Secretary prescribing that the manufacturer is required under this section to conduct such surveillance, submit, for the approval of the Secretary, a plan for the required surveillance. The Secretary, within 60 days of the receipt of such plan, shall determine if the person designated to conduct the surveillance has appropriate qualifications and experience to undertake such surveillance and if the plan will result in the collection of useful data that can reveal unforeseen adverse events or other information necessary to protect the public health. [The Secretary, in consultation] *Except as provided in paragraph (2), the Secretary, in consultation* with the manufacturer, may by order require a prospective surveillance period of up to 36 months. [Any determination] *Except as provided in paragraph (2), any determination* by the Secretary that a longer period is necessary shall be made by mutual agreement between the Secretary and the manufacturer or, if no agreement can be reached, after the completion of a dispute resolution process as described in section 562.

(2) LONGER STUDIES FOR PEDIATRIC DEVICES.—The Secretary may by order require a prospective surveillance period of more than 36 months with respect to a device that is expected to have significant use in pediatric populations if such period of more than 36 months is necessary in order to assess the impact of the device on growth and development, or the effects of growth, development, activity level, or other factors on the safety or efficacy of the device.

(c) DISPUTE RESOLUTION.—A manufacturer may request review under section 562 of any order or condition requiring postmarket surveillance under this section. During the pendency of such review, the device subject to such a postmarket surveillance order or condition shall not be deemed misbranded under section 502(t) or otherwise in violation of such order or condition or a related requirement of this Act unless deemed necessary to protect the public health.

SEC. 523. ACCREDITED PERSONS.

(a) * * *

* * * * * * *

(c) DURATION.—The authority provided by this section terminates October 1, [2007] *2012*.

* * * * * * *

SUBCHAPTER E—GENERAL PROVISIONS RELATING TO DRUGS AND DEVICES

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SEC. 566. CRITICAL PATH PUBLIC-PRIVATE PARTNERSHIPS.

(a) ESTABLISHMENT.—The Secretary, acting through the Commissioner of Food and Drugs, shall enter into collaborative agreements, to be known as Critical Path Public-Private Partnerships, with one or more eligible entities to implement the Critical Path Initiative of the Food and Drug Administration by developing innovative, col-

laborative projects in research, education, and outreach for the purpose of fostering medical product innovation, enabling the acceleration of medical product development, and enhancing medical product safety.

(b) ELIGIBLE ENTITY.—In this section, the term "eligible entity" means an entity that meets each of the following:

(1) The entity is—

(A) an institution of higher education (as such term is defined in section 101 of the Higher Education Act of 1965); or

(B) an organization described in section 501(c)(3) of the Internal Revenue Code of 1986 and exempt from tax under section 501(a) of such Code.

(2) The entity has experienced personnel and clinical and other technical expertise in the biomedical sciences.

(3) The entity demonstrates to the Secretary's satisfaction that the entity is capable of—

(A) developing and critically evaluating tools, methods, and processes—

(i) to increase efficiency, predictability, and productivity of medical product development; and

(ii) to more accurately identify the benefits and risks of new and existing medical products;

(B) establishing partnerships, consortia, and collaborations with health care practitioners and other providers of health care goods or services; pharmacists; pharmacy benefit managers and purchasers; health maintenance organizations and other managed health care organizations; health care insurers; government agencies; patients and consumers; manufacturers of prescription drugs, biological products, diagnostic technologies, and devices; and academic scientists; and

(C) securing funding for the projects of a Critical Path Public-Private Partnership from Federal and nonfederal governmental sources, foundations, and private individuals.

(c) FUNDING.—The Secretary may not enter into a collaborative agreement under subsection (a) unless the eligible entity involved provides an assurance that the entity will not accept funding for a Critical Path Public-Private Partnership project from any organization that manufactures or distributes products regulated by the Food and Drug Administration unless—

(1) the entity accepts such funding for such project from 2 or more such organizations; and

(2) the entity provides assurances in its agreement with the Food and Drug Administration that the results of the Critical Path Public-Private Partnership project will not be influenced by any source of funding.

(d) ANNUAL REPORT.—Not later than 18 months after the date of the enactment of this section, and annually thereafter, the Secretary, in collaboration with the parties to each Critical Path Public-Private Partnership, shall submit a report to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives—

(1) reviewing the operations and activities of the Partnerships in the previous year; and

(2) addressing such other issues relating to this section as the Secretary determines to be appropriate.

(e) DEFINITION.—In this section, the term "medical product" includes a drug, a biological product, a device, and any combination of such products.

(f) AUTHORIZATION OF APPROPRIATIONS.—To carry out this section, there are authorized to be appropriated $5,000,000 for fiscal year 2008 and such sums as may be necessary for each of fiscal years 2009 through 2012.

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CHAPTER VII—GENERAL AUTHORITY

SUBCHAPTER A—General Administrative Provisions

* * * * * * *

FACTORY INSPECTION

SEC. 704. (a) * * *

* * * * * * *

(g)(1) [Not later than one year after the date of the enactment of this subsection, the Secretary] *The Secretary* shall, subject to the provisions of this subsection, accredit persons for the purpose of conducting inspections of establishments that manufacture, prepare, propagate, compound, or process class II or class III devices, which inspections are required under section 510(h) or are inspections of such establishments required to register under section 510(i). The owner or operator of such an establishment that is eligible under paragraph (6) may, from the list published under paragraph (4), select an accredited person to conduct such inspections.

(2) [Not later than 180 days after the date of enactment of this subsection, the Secretary] *The Secretary* shall publish in the Federal Register criteria to accredit or deny accreditation to persons who request to perform the duties specified in paragraph (1). Thereafter, the Secretary shall inform those requesting accreditation, within 60 days after the receipt of such request, whether the request for accreditation is adequate for review, and the Secretary shall promptly act on the request for accreditation. Any resulting accreditation shall state that such person is accredited to conduct inspections at device establishments identified in paragraph (1). The accreditation of such person shall specify the particular activities under this subsection for which such person is accredited. [In the first year following the publication in the Federal Register of criteria to accredit or deny accreditation to persons who request to perform the duties specified in paragraph (1), the Secretary shall accredit no more than 15 persons who request to perform duties specified in paragraph (1).]

(3) An accredited person shall, at a minimum, meet the following requirements:

(A) * * *

* * * * * * *

(F) Such person shall notify the Secretary of any withdrawal, suspension, restriction, or expiration of certificate of conformance with the quality systems standard referred to in paragraph (7) for any device establishment that such person inspects under this subsection not later than 30 days after such withdrawal, suspension, restriction, or expiration.

(G) Such person may conduct audits to establish conformance with the quality systems standard referred to in paragraph (7).

* * * * * * *

[(6)(A) Subject to subparagraphs (B) and (C), a device establishment is eligible for inspections by persons accredited under paragraph (2) if the following conditions are met:

[(i) The Secretary classified the results of the most recent inspection described in paragraph (1) as "no action indicated" or "voluntary action indicated".

[(ii) With respect to inspections to be conducted by an accredited person during a 2-year period—

[(I) the owner or operator of the establishment submits to the Secretary a notice requesting clearance to use an accredited person to conduct the inspection, and the Secretary provides such clearance; and

[(II) such notice identifies the accredited person whom the establishment has selected to conduct the inspection, and the Secretary agrees to the selected accredited person.

[(iii) With respect to the devices that are manufactured, prepared, propagated, compounded, or processed by the establishment, at least one of such devices is marketed in the United States, and 1 or both of the following additional conditions are met:

[(I) At least one of such devices is marketed, or is intended to be marketed, in one or more foreign countries, one of which countries certifies, accredits, or otherwise recognizes the person (accredited under paragraph (2) and identified under clause (ii)(II)) as a person authorized to conduct such inspections of device establishments.

[(II) The owner or operator of the establishment submits to the Secretary a statement that the law of a country in which such a device is marketed, or is intended to be marketed, recognizes an inspection of the establishment by the Secretary or by a person accredited under paragraph (2), and not later than 30 days after receiving such statement, the Secretary informs the owner or operator of the establishment that the owner or operator may submit a notice requesting clearance under clause (ii).

[(iv)(I) In the case of an inspection to be conducted pursuant to section 510(h), persons accredited under paragraph (2) did not conduct inspections of the establishment during the previous 4 years, except that the establishment may petition the Secretary for a waiver of such condition. Such a waiver may be granted only if the petition states a commercial reason for the waiver; the Secretary determines that the public health would be served by granting the waiver; and the Secretary has conducted an inspection of the establishment during the four-year period preceding the date on which the notice under clause (ii) is submitted to the Secretary. Such a waiver is

deemed to be granted only if the Secretary has not determined that the public health would not be served by granting the waiver; and the owner or operator of the device establishment has requested in writing, not later than 18 months following the most recent inspection of such establishment by a person accredited under paragraph (2), that the Secretary inspect the establishment and the Secretary has not conducted an inspection within 30 months after the most recent inspection. With respect to such a waiver that is granted or deemed to be granted, no additional such waiver may be granted or deemed to be granted until after the Secretary has conducted an inspection of the establishment.

[(II) In the case of an inspection to be conducted of a device establishment required to register pursuant to section 510(i), the Secretary periodically conducts inspections of the establishment.

[(B)(i) The Secretary shall respond to a notice under subparagraph (A) from a device establishment not later than 30 days after the Secretary receives the notice. Through such response, the Secretary shall (I) provide clearance under such subparagraph, and agree to the selection of an accredited person, or (II) make a request under clause (ii). If the Secretary fails to respond to the notice within such 30-day period, the establishment is deemed to have such clearance, and to have the agreement of the Secretary for such selection.

[(ii) The request referred to in clause (i)(II) is—

[(I) a request to the device establishment involved to submit to the Secretary compliance data in accordance with clause (iii); or

[(II) a request to the establishment, or to the accredited person identified in the notice under subparagraph (A), for information concerning the relationship between the establishment and such accredited person, including information about the number of inspections of the establishment, or other establishments owned or operated by the owner or operator of the establishment, that have been conducted by the accredited person.

The Secretary may make both such requests.

[(iii) The compliance data to be submitted by a device establishment under clause (ii) are data describing whether the quality controls of the establishment have been sufficient for ensuring consistent compliance with current good manufacturing practice within the meaning of section 501(h) and with other applicable provisions of this Act. Such data shall include complete reports of inspectional findings regarding good manufacturing practice or other quality control audits that, during the preceding two-year period, were conducted at the establishment by persons other than the owner or operator of the establishment, together with all other relevant compliance data the Secretary deems necessary. Data under the preceding sentence shall demonstrate to the Secretary whether the establishment has facilitated consistent compliance by promptly correcting any compliance problems identified in such inspections.

[(iv)(I) Not later than 60 days after receiving compliance data under clause (iii) from a device establishment, the Secretary shall

provide or deny clearance under subparagraph (A). The Secretary may deny clearance if the Secretary determines that the establishment has failed to demonstrate consistent compliance for purposes of clause (iii). The Secretary shall provide to the establishment a statement of such reasons for such determination. If the Secretary fails to provide such statement to the establishment within such 60-day period, the establishment is deemed to have such clearance.

[(II) If, during the two-year period following clearance under subparagraph (A), the Secretary determines that the device establishment is substantially not in compliance with this Act, the Secretary may, after notice and a written response, notify the establishment that the eligibility of the establishment for the inspections by accredited persons has been suspended.

[(v)(I) A request to an accredited person under clause (ii)(II) may not seek any information that is not required to be maintained by such person in records under subsection (f)(1). Not later than 60 days after receiving the information sought by the request, the Secretary shall agree to, or reject, the selection of such person by the device establishment involved. The Secretary may reject the selection if the Secretary provides to the establishment a statement of the reasons for such rejection. Reasons for the rejection may include that the establishment or the accredited person, as the case may be, has failed to fully respond to the request, or that the Secretary has concerns regarding the relationship between the establishment and such accredited person. If within such 60-day period the Secretary fails to agree to or reject the selection in accordance with this subclause, the Secretary is deemed to have agreed to the selection.

[(II) If the Secretary rejects the selection of an accredited person by a device establishment, the establishment may make an additional selection of an accredited person by submitting to the Secretary a notice that identifies the additional selection. Clauses (i) and (ii), and subclause (I) of this clause, apply to the selection of an accredited person through a notice under the preceding sentence in the same manner and to the same extent as such provisions apply to a selection of an accredited person through a notice under subparagraph (A).

[(vi) In the case of a device establishment that under clause (iv) is denied clearance under subparagraph (A), or whose selection of an accredited person is rejected under clause (v), the Secretary shall designate a person to review the findings of the Secretary under such clause if, during the 30-day period beginning on the date on which the establishment receives the findings, the establishment requests the review. The review shall commence not later than 30 days after the establishment requests the review, unless the Secretary and the establishment otherwise agree.

[(C)(i) In the case of a device establishment for which the Secretary classified the results of the most recent inspection of the establishment by a person accredited under paragraph (2) as "official action indicated", the establishment, if otherwise eligible under subparagraph (A), is eligible for further inspections by persons accredited under such paragraph if (I) the Secretary issues a written statement to the owner or operator of the establishment that the violations leading to such classification have been resolved, and (II) the Secretary, either upon the Secretary's own initiative or a peti-

tion of the owner or operator of the establishment, notifies the establishment that it has clearance to use an accredited person for the inspections. The Secretary shall respond to such petition within 30 days after the receipt of the petition.

[(ii) If the Secretary denies a petition under clause (i), the device establishment involved may, after the expiration of one year after such denial, again petition the Secretary for a determination of eligibility for inspection by persons accredited by the Secretary under paragraph (2). If the Secretary denies such petition, the Secretary shall provide the establishment with such reasons for such denial within 60 days after the denial. If, as of the expiration of 48 months after the receipt of the first petition, the establishment has not been inspected by the Secretary, the establishment is eligible for further inspections by accredited persons.**]**

(6)(A) Subject to subparagraphs (B) and (C), a device establishment is eligible for inspection by persons accredited under paragraph (2) if the following conditions are met:

(i) The Secretary classified the results of the most recent inspection of the establishment as "no action indicated" or "voluntary action indicated".

(ii) With respect to inspections of the establishment to be conducted by an accredited person, the owner or operator of the establishment submits to the Secretary a notice that—

(I) provides the date of the last inspection of the establishment by the Secretary and the classification of that inspection;

(II) states the intention of the owner or operator to use an accredited person to conduct inspections of the establishment;

(III) identifies the particular accredited person the owner or operator intends to select to conduct such inspections; and

(IV) includes a certification that, with respect to the devices that are manufactured, prepared, propagated, compounded, or processed in the establishment—

(aa) at least 1 of such devices is marketed in the United States; and

(bb) at least 1 of such devices is marketed, or is intended to be marketed, in 1 or more foreign countries, 1 of which countries certifies, accredits, or otherwise recognizes the person accredited under paragraph (2) and identified under subclause (III) as a person authorized to conduct inspections of device establishments.

(B)(i) Except with respect to the requirement of subparagraph (A)(i), a device establishment is deemed to have clearance to participate in the program and to use the accredited person identified in the notice under subparagraph (A)(ii) for inspections of the establishment unless the Secretary, not later than 30 days after receiving such notice, issues a response that—

(I) denies clearance to participate as provided under subparagraph (C); or

(II) makes a request under clause (ii).

(ii) The Secretary may request from the owner or operator of a device establishment in response to the notice under subpara-

graph (a)(ii) with respect to the establishment, or from the particular accredited person identified in such notice—

(I) compliance data for the establishment in accordance with clause (iii)(I); or

(II) information concerning the relationship between the owner or operator of the establishment and the accredited person identified in such notice in accordance with clause (iii)(II).

The owner or operator of the establishment, or such accredited person, as the case may be, shall respond to such a request not later than 60 days after receiving such request.

(iii)(I) The compliance data to be submitted by the owner or operation of a device establishment in response to a request under clause (ii)(I) are data describing whether the quality controls of the establishment have been sufficient for ensuring consistent compliance with current good manufacturing practice within the meaning of section 501(h) and with other applicable provisions of this Act. Such data shall include complete reports of inspectional findings regarding good manufacturing practice or other quality control audits that, during the preceding 2-year period, were conducted at the establishment by persons other than the owner or operator of the establishment, together with all other compliance data the Secretary deems necessary. Data under the preceding sentence shall demonstrate to the Secretary whether the establishment has facilitated consistent compliance by promptly correcting any compliance problems identified in such inspections.

(II) A request to an accredited person under clause (ii)(II) may not seek any information that is not required to be maintained by such person in records under subsection (f)(1).

(iv) A device establishment is deemed to have clearance to participate in the program and to use the accredited person identified in the notice under subparagraph (A)(ii) for inspections of the establishment unless the Secretary, not later than 60 days after receiving the information requested under clause (ii), issues a response that denies clearance to participate as provided under subparagraph (C).

(C)(i) The Secretary may deny clearance to a device establishment if the Secretary has evidence that the certification under subparagraph (A)(ii)(IV) is untrue and the Secretary provides to the owner or operator of the establishment a statement summarizing such evidence.

(ii) The Secretary may deny clearance to a device establishment if the Secretary determines that the establishment has failed to demonstrate consistent compliance for purposes of subparagraph (B)(iii)(I) and the Secretary provides to the owner or operator of the establishment a statement of the reasons for such determination.

(iii)(I) The Secretary may reject the selection of the accredited person identified in the notice under subparagraph (A)(ii) if the Secretary provides to the owner or operator of the establishment a statement of the reasons for such rejection. Reasons for the rejection may include that the establishment or the accredited

person, as the case may be, has failed to fully respond to the request, or that the Secretary has concerns regarding the relationship between the establishment and such accredited person.

(II) If the Secretary rejects the selection of an accredited person by the owner or operator of a device establishment, the owner or operator may make an additional selection of an accredited person by submitting to the Secretary a notice that identifies the additional selection. Clauses (i) and (ii) of subparagraph (B), and subclause (I) of this clause, apply to the selection of an accredited person through a notice under the preceding sentence in the same manner and to the same extent as such provisions apply to a selection of an accredited person through a notice under subparagraph (A)(ii).

(iv) In the case of a device establishment that is denied clearance under clause (i) or (ii) or with respect to which the selection of the accredited person is rejected under clause (iii), the Secretary shall designate a person to review the statement of reasons, or statement summarizing such evidence, as the case may be, of the Secretary under such clause if, during the 30-day period beginning on the date on which the owner or operator of the establishment receives such statement, the owner or operator requests the review. The review shall commence not later than 30 days after the owner or operator requests the review, unless the Secretary and the owner or operator otherwise agree.

(7)**[**(A) Persons accredited under paragraph (2) to conduct inspections shall record in writing their inspection observations and shall present the observations to the device establishment's designated representative and describe each observation. Additionally, such accredited person shall prepare an inspection report (including for inspections classified as "no action indicated") in a form and manner consistent with such reports prepared by employees and officials designated by the Secretary to conduct inspections.**]** *(A) Persons accredited under paragraph (2) to conduct inspections shall record in writing their inspection observations and shall present the observations to the device establishment's designated representative and describe each observation. Additionally, such accredited person shall prepare an inspection report in a form and manner designated by the Secretary to conduct inspections, taking into consideration the goals of international harmonization of quality systems standards. Any official classification of the inspection shall be determined by the Secretary.*

* * * * * * *

(F) For the purpose of setting risk-based inspectional priorities, the Secretary shall accept voluntary submissions of reports of audits assessing conformance with appropriate quality systems standards set by the International Organization for Standardization (ISO) and identified by the Secretary in public notice. If the owner or operator of an establishment elects to submit audit reports under this subparagraph, the owner or operator shall submit all such audit reports with respect to the establishment during the preceding 2-year periods.

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(10)(A) * * *

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(C) For purposes of this paragraph:

(i) * * *

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(iii) The term "adjusted base amount", with respect to applicability to fiscal year 2004 or any subsequent fiscal year, means the adjusted [based] *base* amount applicable to the preceding year increased by 5 percent.

* * * * * * *

SEC. 712. CONFLICTS OF INTEREST.

(a) DEFINITIONS.—For purposes of this section:

(1) ADVISORY COMMITTEE.—The term "advisory committee" means an advisory committee under the Federal Advisory Committee Act that provides advice or recommendations to the Secretary regarding activities of the Food and Drug Administration.

(2) FINANCIAL INTEREST.—The term "financial interest" means a financial interest under section 208(a) of title 18, United States Code.

(b) APPOINTMENTS TO ADVISORY COMMITTEES.—

(1) RECRUITMENT.—

(A) IN GENERAL.—Given the importance of advisory committees to the review process at the Food and Drug Administration, the Secretary, through the Office of Women's Health, the Office of Orphan Product Development, the Office of Pediatric Therapeutics, and other offices within the Food and Drug Administration with relevant expertise, shall develop and implement strategies on effective outreach to potential members of advisory committees at universities, colleges, other academic research centers, professional and medical societies, and patient and consumer groups. The Secretary shall seek input from professional medical and scientific societies to determine the most effective informational and recruitment activities. The Secretary shall also take into account the advisory committees with the greatest number of vacancies.

(B) RECRUITMENT ACTIVITIES.—The recruitment activities under subparagraph (A) may include—

(i) advertising the process for becoming an advisory committee member at medical and scientific society conferences;

(ii) making widely available, including by using existing electronic communications channels, the contact information for the Food and Drug Administration point of contact regarding advisory committee nominations; and

(iii) developing a method through which an entity receiving funding from the National Institutes of Health, the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, or the Veterans Health Administration can identify a person who the Food and Drug Administration can contact regard-

ing the nomination of individuals to serve on advisory committees.

(2) EVALUATION AND CRITERIA.—When considering a term appointment to an advisory committee, the Secretary shall review the expertise of the individual and the financial disclosure report filed by the individual pursuant to the Ethics in Government Act of 1978 for each individual under consideration for the appointment, so as to reduce the likelihood that an appointed individual will later require a written determination as referred to in section 208(b)(1) of title 18, United States Code, a written certification as referred to in section 208(b)(3) of title 18, United States Code, or a waiver as referred to in subsection (c)(3) of this section for service on the committee at a meeting of the committee.

(3) PARTICIPATION OF GUEST EXPERT WITH FINANCIAL INTEREST.—Notwithstanding any other provision of this section, an individual with a financial interest with respect to any matter considered by an advisory committee may be allowed to participate in a meeting of an advisory committee as a guest expert if the Secretary determines that the individual has particular expertise required for the meeting. An individual participating as a guest expert may provide information and expert opinion, but shall not participate in the discussion or voting by the members of the advisory committee.

(c) GRANTING AND DISCLOSURE OF WAIVERS.—

(1) IN GENERAL.—Prior to a meeting of an advisory committee regarding a "particular matter" (as that term is used in section 208 of title 18, United States Code), each member of the committee who is a full-time Government employee or special Government employee shall disclose to the Secretary financial interests in accordance with subsection (b) of such section 208.

(2) FINANCIAL INTEREST OF ADVISORY COMMITTEE MEMBER OR FAMILY MEMBER.—No member of an advisory committee may vote with respect to any matter considered by the advisory committee if such member (or an immediate family member of such member) has a financial interest that could be affected by the advice given to the Secretary with respect to such matter, excluding interests exempted in regulations issued by the Director of the Office of Government Ethics as too remote or inconsequential to affect the integrity of the services of the Government officers or employees to which such regulations apply.

(3) WAIVER.—The Secretary may grant a waiver of the prohibition in paragraph (2) if such waiver is necessary to afford the advisory committee essential expertise.

(4) LIMITATIONS.—

(A) ONE WAIVER PER COMMITTEE MEETING.—Notwithstanding any other provision of this section, with respect to each advisory committee, the Secretary shall not grant more than 1 waiver under paragraph (3) per committee meeting.

(B) SCIENTIFIC WORK.—The Secretary may not grant a waiver under paragraph (3) for a member of an advisory committee when the member's own scientific work is involved.

(5) DISCLOSURE OF WAIVER.—Notwithstanding section 107(a)(2) of the Ethics in Government Act (5 U.S.C. App.), the following shall apply:

(A) 15 OR MORE DAYS IN ADVANCE.—As soon as practicable, but in no case later than 15 days prior to a meeting of an advisory committee to which a written determination as referred to in section 208(b)(1) of title 18, United States Code, a written certification as referred to in section 208(b)(3) of title 18, United States Code, or a waiver as referred to in paragraph (3) applies, the Secretary shall disclose (other than information exempted from disclosure under section 552 of title 5, United States Code, and section 552a of title 5, United States Code (popularly known as the Freedom of Information Act and the Privacy Act of 1974, respectively)) on the Internet website of the Food and Drug Administration—

(i) the type, nature, and magnitude of the financial interests of the advisory committee member to which such determination, certification, or waiver applies; and

(ii) the reasons of the Secretary for such determination, certification, or waiver.

(B) LESS THAN 30 DAYS IN ADVANCE.—In the case of a financial interest that becomes known to the Secretary less than 30 days prior to a meeting of an advisory committee to which a written determination as referred to in section 208(b)(1) of title 18, United States Code, a written certification as referred to in section 208(b)(3) of title 18, United States Code, or a waiver as referred to in paragraph (3) applies, the Secretary shall disclose (other than information exempted from disclosure under section 552 of title 5, United States Code, and section 552a of title 5, United States Code) on the Internet website of the Food and Drug Administration, the information described in clauses (i) and (ii) of subparagraph (A) as soon as practicable after the Secretary makes such determination, certification, or waiver, but in no case later than the date of such meeting.

(d) PUBLIC RECORD.—The Secretary shall ensure that the public record and transcript of each meeting of an advisory committee includes the disclosure required under subsection (c)(5) (other than information exempted from disclosure under section 552 of title 5, United States Code, and section 552a of title 5, United States Code).

(e) ANNUAL REPORT.—Not later than February 1 of each year, the Secretary shall submit to the Committee on Appropriations and the Committee on Health, Education, Labor, and Pensions of the Senate, and the Committee on Appropriations and the Committee on Energy and Commerce of the House of Representatives a report that describes—

(1) with respect to the fiscal year that ended on September 30 of the previous year, the number of vacancies on each advisory committee, the number of nominees received for each committee, and the number of such nominees willing to serve;

(2) with respect to such year, the aggregate number of disclosures required under subsection (c)(5) for each meeting of each advisory committee and the percentage of individuals to whom

such disclosures did not apply who served on such committee for each such meeting;

(3) with respect to such year, the number of times the disclosures required under subsection (c)(5) occurred under subparagraph (B) of such subsection; and

(4) how the Secretary plans to reduce the number of vacancies reported under paragraph (1) during the fiscal year following such year, and mechanisms to encourage the nomination of individuals for service on an advisory committee, including those who are classified by the Food and Drug Administration as academicians or practitioners.

(f) PERIODIC REVIEW OF GUIDANCE.—Not less than once every 5 years, the Secretary shall review guidance of the Food and Drug Administration regarding conflict of interest waiver determinations with respect to advisory committees and update such guidance as necessary.

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SUBCHAPTER C—FEES

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PART 2—FEES RELATING TO DRUGS

SEC. 735. DEFINITIONS.

For purposes of this subchapter:

(1) The term "human drug application" means an application for—

(A) approval of a new drug submitted under section [505(b)(1),] *505(b), or*

[(B) approval of a new drug submitted under section 505(b)(2) after September 30, 1992, which requests approval of—

[(i) a molecular entity which is an active ingredient (including any salt or ester of an active ingredient), or

[(ii) an indication for a use,

that had not been approved under an application submitted under section 505(b), or]

[(C)] *(B)* licensure of a biological product under section 351 of the Public Health Service Act.

* * * * * * *

(3) The term "prescription drug product" means a specific strength or potency of a drug in final dosage form—

(A) * * *

* * * * * * *

(C) which is on the list of products described in section [505(j)(7)(A)] *505(j)(7)(A) (not including the discontinued section of such list),* or is on a list created and maintained by the Secretary of products approved under human drug applications under section 351 of the Public Health Service Act *(not including the discontinued section of such list)*.

* * * * * * *

(4) The term "final dosage form" means, with respect to a prescription drug product, a finished dosage form which is approved for administration to a patient without substantial further manufacturing *(such as capsules, tablets, or lyophilized products before reconstitution)*.

* * * * * * *

(6) The term "process for the review of human drug applications" means the following activities of the Secretary with respect to the review of human drug applications and supplements:

(A) * * *

* * * * * * *

[(F) In the case of drugs approved after October 1, 2002, under human drug applications or supplements: collecting, developing, and reviewing safety information on the drugs, including adverse event reports, during a period of time after approval of such applications or supplements, not to exceed three years.]

(F) Postmarket safety activities with respect to drugs approved under human drug applications or supplements, including the following activities:

(i) Collecting, developing, and reviewing safety information on approved drugs, including adverse event reports.

(ii) Developing and using improved adverse-event data-collection systems, including information technology systems.

(iii) Developing and using improved analytical tools to assess potential safety problems, including access to external data bases.

(iv) Preparing and making publicly available (including on the website of the Food and Drug Administration) a summary analysis of the adverse drug reaction reports received for recently approved drugs, including identification of any new risks not previously identified, potential new risks, or known risks reported in unusual number not previously identified within 18 months of the drug's initial marketing or after exposure of 10,000 individuals to the drug, whichever is later.

(v) Conducting regular, bi-weekly screening of the Adverse Event Reporting System database and developing a report every 15 days on any new safety concerns.

(vi) Ensuring that the reports available to the public under the Adverse Event Reporting System are updated at least every 6 months.

(vii) Reporting to the Congress on—

(I) the recommendations received in consultations with, and reports from, the Office of Surveillance and Epidemiology within the Food and Drug Administration on postmarket safety activities;

(II) a description of the actions taken on those recommendations; and

(III) if no action is taken, or a different action is taken relative to the action recommended by the Office of Surveillance and Epidemiology, an explanation of why no action or a different action was taken.

(viii) On an annual basis, reviewing the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, reporting to the Congress on these determinations, and assigning start dates and estimated completion dates for such commitments.

(ix) Developing postmarket safety performance measures, including those listed in clauses (iv) through (viii), that are as measurable and rigorous as the ones already developed for premarket review.

(G) Activities relating to the support of studies of drugs on pediatric populations under section 505A(n)(1).

* * * * * * *

(8) The term "adjustment factor" applicable to a fiscal year is the Consumer Price Index for all urban consumers (all items; United States city average) for [April of the preceding fiscal year] *October of the preceding fiscal year* divided by such Index for [April 1997] *October 1996*.

(9) The term "person" includes an affiliate thereof.

(10) The term "active", with respect to a commercial investigational new drug application, means such an application to which information was submitted during the relevant period.

[(9)] *(11)* The term "affiliate" means a business entity that has a relationship with a second business entity if, directly or indirectly—

(A) * * *

* * * * * * *

SEC. 736. AUTHORITY TO ASSESS AND USE DRUG FEES.

(a) TYPES OF FEES.—Beginning in fiscal year [2003] *2008*, the Secretary shall assess and collect fees in accordance with this section as follows:

(1) HUMAN DRUG APPLICATION AND SUPPLEMENT FEE.—

(A) IN GENERAL.—Each person that submits, on or after September 1, 1992, a human drug application or a supplement shall be subject to a fee as follows:

(i) A fee established under subsection [(c)(4)] *(c)(5)* for a human drug application for which clinical data (other than bioavailability or bioequivalence studies) with respect to safety or effectiveness are required for approval.

(ii) A fee established under subsection [(c)(4)] *(c)(5)* for a human drug application for which clinical data with respect to safety or effectiveness are not required or a supplement for which clinical data (other than bioavailability or bioequivalence studies) with respect to safety or effectiveness are required. Such fee shall

be half of the amount of the fee established under clause (i).

* * * * * * *

(D) REFUND OF FEE IF APPLICATION REFUSED FOR FILING *OR WITHDRAWN BEFORE FILING*.—The Secretary shall refund 75 percent of the fee paid under subparagraph (B) for any application or supplement which is refused for filing *or withdrawn without a waiver before filing*.

(E) FEES FOR APPLICATIONS PREVIOUSLY REFUSED FOR FILING OR WITHDRAWN BEFORE FILING.—A human drug application or supplement that was submitted but was refused for filing, or was withdrawn before being accepted or refused for filing, shall be subject to the full fee under subparagraph (A) upon being resubmitted or filed over protest, unless the fee is waived or reduced under subsection (d).

[(E)] *(F)* EXCEPTION FOR DESIGNATED ORPHAN DRUG OR INDICATION.—A human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition pursuant to section 526 shall not be subject to a fee under subparagraph (A), unless the human drug application includes an indication for other than a rare disease or condition. A supplement proposing to include a new indication for a rare disease or condition in a human drug application shall not be subject to a fee under subparagraph (A), if the drug has been designated pursuant to section 526 as a drug for a rare disease or condition with regard to the indication proposed in such supplement.

[(F)] *(G)* REFUND OF FEE IF APPLICATION WITHDRAWN.—If an application or supplement is withdrawn after the application or supplement was filed, the Secretary may refund the fee or a portion of the fee if no substantial work was performed on the application or supplement after the application or supplement was filed. The Secretary shall have the sole discretion to refund a fee or a portion of the fee under this subparagraph. A determination by the Secretary concerning a refund under this paragraph shall not be reviewable.

(2) PRESCRIPTION DRUG ESTABLISHMENT FEE.—

(A) IN GENERAL.—Except as provided in [subparagraph (B)] *subparagraphs (B) and (C)*, each person that—

(i) * * *

* * * * * * *

shall be assessed an annual fee established under subsection [(c)(4)] *(c)(5)* for each prescription drug establishment listed in its approved human drug application as an establishment that manufactures the prescription drug product named in the application. The annual establishment fee shall be assessed in each fiscal year in which the prescription drug product named in the application is assessed a fee under paragraph (3) unless the prescription drug establishment listed in the application does not engage in the manufacture of the prescription drug product during the fiscal year. The establishment fee shall be payable on or before October 1 of each year. Each such estab-

lishment shall be assessed only one fee per establishment, notwithstanding the number of prescription drug products manufactured at the establishment. In the event an establishment is listed in a human drug application by more than one applicant, the establishment fee for the fiscal year shall be divided equally and assessed among the applicants whose prescription drug products are manufactured by the establishment during the fiscal year and assessed product fees under paragraph (3).

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(C) SPECIAL RULES FOR POSITRON EMISSION TOMOGRAPHY DRUGS.—

(i) IN GENERAL.—Except as provided in clause (ii), each person who is named as the applicant in an approved human drug application for a positron emission tomography drug shall be subject under subparagraph (A) to one-sixth of an annual establishment fee with respect to each such establishment identified in the application as producing positron emission tomography drugs under the approved application.

(ii) EXCEPTION FROM ANNUAL ESTABLISHMENT FEE.—Each person who is named as the applicant in an application described in clause (i) shall not be assessed an annual establishment fee for a fiscal year if the person certifies to the Secretary, at a time specified by the Secretary and using procedures specified by the Secretary, that—

(I) the person is a not-for-profit medical center that has only 1 establishment for the production of positron emission tomography drugs; and

(II) at least 95 percent of the total number of doses of each positron emission tomography drug produced by such establishment during such fiscal year will be used within the medical center.

(iii) DEFINITION.—For purposes of this subparagraph, the term "positron emission tomography drug" has the meaning given to the term "compounded positron emission tomography drug" in section 201(ii), except that subparagraph (1)(B) of such section shall not apply.

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(3) PRESCRIPTION DRUG PRODUCT FEE.—

(A) IN GENERAL.—Except as provided in subparagraph (B), each person who is named as the applicant in a human drug application, and who, after September 1, 1992, had pending before the Secretary a human drug application or supplement, shall pay for each such prescription drug product the annual fee established under subsection ⟦(c)(4)⟧ *(c)(5)*. Such fee shall be payable on or before October 1 of each year. Such fee shall be paid only once for each product for a fiscal year in which the fee is payable.

* * * * * * *

[(b) FEE REVENUE AMOUNTS.—Except as provided in subsections (c), (d), (f), and (g), fees under subsection (a) shall be established to generate the following revenue amounts:

[Type of Fee Revenue	Fiscal Year 2003	Fiscal Year 2004	Fiscal Year 2005	Fiscal Year 2006	Fiscal Year 2007
Application/Supplement	$74,300,000	$77,000,000	$84,000,000	$86,434,000	$86,434,000
Establishment	$74,300,000	$77,000,000	$84,000,000	$86,433,000	$86,433,000
Product	$74,300,000	$77,000,000	$84,000,000	$86,433,000	$86,433,000
Total Fee Revenue	$222,900,000	$231,000,000	$252,000,000	$259,300,000	$259,300,000

If, after the date of the enactment of the Prescription Drug User Fee Amendments of 2002 , legislation is enacted requiring the Secretary to fund additional costs of the retirement of Federal personnel, fee revenue amounts shall be increased in each year by the amount necessary to fully fund the portion of such additional costs that are attributable to the process for the review of human drug applications.]

(b) FEE REVENUE AMOUNTS.—

(1) IN GENERAL.—For each of the fiscal years 2008 through 2012, fees under subsection (a) shall, except as provided in subsections (c), (d), (f), and (g), be established to generate a total revenue amount under such subsection that is equal to the sum of—

(A) $392,783,000; and

(B) an amount equal to the modified workload adjustment factor for fiscal year 2007 (as determined under paragraph (3)).

(2) TYPES OF FEES.—Of the total revenue amount determined for a fiscal year under paragraph (1)—

(A) one-third shall be derived from fees under subsection (a)(1) (relating to human drug applications and supplements);

(B) one-third shall be derived from fees under subsection (a)(2) (relating to prescription drug establishments); and

(C) one-third shall be derived from fees under subsection (a)(3) (relating to prescription drug products).

(3) MODIFIED WORKLOAD ADJUSTMENT FACTOR FOR FISCAL YEAR 2007.—For purposes of paragraph (1)(B), the Secretary shall determine the modified workload adjustment factor by determining the dollar amount that results from applying the methodology that was in effect under subsection (c)(2) for fiscal year 2007 to the amount $354,893,000, except that, with respect to the portion of such determination that is based on the change in the total number of commercial investigational new drug applications, the Secretary shall count the number of such applications that were active during the most recent 12-month period for which data on such submissions is available.

(4) ADDITIONAL FEE REVENUES FOR DRUG SAFETY.—

(A) IN GENERAL.—For each of the fiscal years 2008 through 2012, paragraph (1)(A) shall, subject to subparagraph (C), be applied by substituting the amount determined under subparagraph (B) for "$392,783,000".

(B) AMOUNT DETERMINED.—For each of the fiscal years 2008 through 2012, the amount determined under this subparagraph is the sum of—

(i) $392,783,000; plus

(ii) an amount equal to—

(I)(aa) for fiscal year 2008, $25,000,000;

(bb) for fiscal year 2009, $35,000,000;

(cc) for fiscal year 2010, $45,000,000;

(dd) for fiscal year 2011, $55,000,000; and

(ee) for fiscal year 2012, $65,000,000; minus

(II) the amount equal to the excess amount in item (bb), provided that—

(aa) the amount of the total appropriation for the Food and Drug Administration for such fiscal year (excluding the amount of fees appropriated for such fiscal year) exceeds the amount of the total appropriation for the Food and Drug Administration for fiscal year 2007 (excluding the amount of fees appropriated for such fiscal year), adjusted as provided under subsection (c)(1); and

(bb) the amount of the total appropriations for the process of human drug review at the Food and Drug Administration for such fiscal year (excluding the amount of fees appropriated for such fiscal year) exceeds the amount of appropriations for the process of human drug review at the Food and Drug Administration for fiscal year 2007 (excluding the amount of fees appropriated for such fiscal year), adjusted as provided under subsection (c)(1).

In making the adjustment under subclause (II) for any of fiscal years 2008 through 2012, subsection (c)(1) shall be applied by substituting "2007" for "2008".

(C) LIMITATION.—This paragraph shall not apply for any fiscal year if the amount described under subparagraph (B)(ii) is less than 0.

(c) ADJUSTMENTS.—

(1) INFLATION ADJUSTMENT.—**[**The revenues established in subsection (b)**]** *For fiscal year 2009 and subsequent fiscal years, the revenues established in subsection (b)* shall be adjusted by the Secretary by notice, published in the Federal Register, for a fiscal year to reflect the greater of—

(A) the total percentage change that occurred in the Consumer Price Index for all urban consumers (all items; U.S. city average) for the 12 month period ending June 30 preceding the fiscal year for which fees are being established, **[**or**]**

(B) the total percentage change for the previous fiscal year in basic pay under the General Schedule in accordance with section 5332 of title 5, United States Code, as adjusted by any locality-based comparability payment pur-

suant to section 5304 of such title for Federal employees stationed in the District of Columbia[.], *or*

(C) the average annual change in the cost, per full-time equivalent position of the Food and Drug Administration, of all personnel compensation and benefits paid with respect to such positions for the first 5 years of the preceding 6 fiscal years.

The adjustment made each fiscal year by this subsection will be added on a compounded basis to the sum of all adjustments made each fiscal year after [fiscal year 2003] *fiscal year 2008* under this subsection.

(2) WORKLOAD ADJUSTMENT.—[Beginning with fiscal year 2004,] *For fiscal year 2009 and subsequent fiscal years,* after the fee revenues established in subsection (b) are adjusted for a fiscal year for inflation in accordance with paragraph (1), the fee revenues shall be adjusted further for such fiscal year to reflect changes in the workload of the Secretary for the process for the review of human drug applications. With respect to such adjustment:

(A) The adjustment shall be determined by the Secretary based on a weighted average of the change in the total number of [human drug applications, commercial investigational new drug applications,] *human drug applications (adjusted for changes in review activities, as described in the notice that the Secretary is required to publish in the Federal Register under this subparagraph),*efficacy supplements, and manufacturing supplements submitted to the Secretary*, and the change in the total number of active commercial investigational new drug applications (adjusted for changes in review activities, as so described) during the most recent 12-month period for which data on such submissions is available*. The Secretary shall publish in the Federal Register the fee revenues and fees resulting from the adjustment and the supporting methodologies.

(B) Under no circumstances shall the adjustment result in fee revenues for a fiscal year that are less than the fee revenues for the fiscal year established in subsection (b), as adjusted for inflation under paragraph (1). *Any adjustment for changes in review activities made in setting fees and revenue amounts for fiscal year 2009 may not result in the total workload adjustment being more than 2 percentage points higher than it would have been in the absence of the adjustment for changes in review activities.*

(C) The Secretary shall contract with an independent accounting firm to study the adjustment for changes in review activities applied in setting fees and revenue amounts for fiscal year 2009 and to make recommendations, if warranted, for future changes in the methodology for calculating the adjustment. After review of the recommendations, the Secretary shall, if warranted, make appropriate changes to the methodology, and the changes shall be effective for each of the fiscal years 2010 through 2012. The Secretary shall not make any adjustment for changes in review activities for any fiscal year after 2009 unless such study has been completed.

(3) RENT AND RENT-RELATED COST ADJUSTMENT.—For fiscal year 2010 and each subsequent fiscal year, the Secretary shall, before making adjustments under paragraphs (1) and (2), decrease the fee revenue amount established in subsection (b) if actual costs paid for rent and rent-related expenses for the preceding fiscal year are less than estimates made for such year in fiscal year 2006. Any reduction made under this paragraph shall not exceed the amount by which such costs fall below the estimates made in fiscal year 2006 for such fiscal year, and shall not exceed $11,721,000 for any fiscal year.

[(3)**]** *(4)* FINAL YEAR ADJUSTMENT.—For fiscal year **[**2007**]** *2012*, the Secretary may, in addition to adjustments under **[**paragraphs (1) and (2)**]** *paragraphs (1), (2), and (3)*, further increase the fee revenues and fees established in subsection (b) if such an adjustment is necessary to provide for not more than three months of operating reserves of carryover user fees for the process for the review of human drug applications for the first three months of fiscal year **[**2008**]** *2013*. If such an adjustment is necessary, the rationale for the amount of the increase shall be contained in the annual notice establishing fee revenues and fees for fiscal year **[**2007**]** *2012*. If the Secretary has carryover balances for such process in excess of three months of such operating reserves, the adjustment under this paragraph shall not be made.

[(4)**]** *(5)* ANNUAL FEE SETTING.—The Secretary shall, 60 days before the start of each fiscal year that begins after September 30, **[**2002**]** *2007*, establish, for the next fiscal year, application, product, and establishment fees under subsection (a), based on the revenue amounts established under subsection (b) and the adjustments provided under this subsection.

[(5)**]** *(6)* LIMIT.—The total amount of fees charged, as adjusted under this subsection, for a fiscal year may not exceed the total costs for such fiscal year for the resources allocated for the process for the review of human drug applications.

(d) FEE WAIVER OR REDUCTION.—

(1) IN GENERAL.—The Secretary shall grant *to a person who is named as the applicant in a human drug application* a waiver from or a reduction of one or more fees assessed *to that person* under subsection (a) where the Secretary finds that—

(A) * * *

* * * * * * *

(2) CONSIDERATIONS.—In determining whether to grant a waiver or reduction of a fee under paragraph (1), the Secretary shall consider only the circumstances and assets of the applicant involved and any affiliate of the applicant.

[(2)**]** *(3)* USE OF STANDARD COSTS.—In making the finding in paragraph (1)(C), the Secretary may use standard costs.

[(3)**]** *(4)* RULES RELATING TO SMALL BUSINESSES.—

(A) DEFINITION.—In paragraph (1)(D), the term "small business" means an entity that has fewer than 500 employees, including employees of affiliates*, and that does not have a drug product that has been approved under a*

human drug application and introduced or delivered for introduction into interstate commerce.

* * * * * * *

(g) CREDITING AND AVAILABILITY OF FEES.—

(1) * * *

* * * * * * *

[(3) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated for fees under this section—

[(A) $222,900,000 for fiscal year 2003;

[(B) $231,000,000 for fiscal year 2004;

[(C) $252,000,000 for fiscal year 2005;

[(D) $259,300,000 for fiscal year 2006; and

[(E) $259,300,000 for fiscal year 2007;

as adjusted to reflect adjustments in the total fee revenues made under this section and changes in the total amounts collected by application, supplement, establishment, and product fees.

[(4) OFFSET.—Any amount of fees collected for a fiscal year under this section that exceeds the amount of fees specified in appropriation Acts for such fiscal year shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be authorized to be collected under this section pursuant to appropriation Acts for a subsequent fiscal year.]

(3) AUTHORIZATION OF APPROPRIATIONS.—For each of the fiscal years 2008 through 2012, there is authorized to be appropriated for fees under this section an amount equal to the total revenue amount determined under subsection (b) for the fiscal year, as adjusted or otherwise affected under subsection (c) and paragraph (4) of this subsection.

(4) OFFSET.—If the sum of the cumulative amount of fees collected under this section for the fiscal years 2008 through 2010 and the amount of fees estimated to be collected under this section for fiscal year 2011 exceeds the cumulative amount appropriated under paragraph (3) for the fiscal years 2008 through 2011, the excess shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be authorized to be collected under this section pursuant to appropriation Acts for fiscal year 2012.

* * * * * * *

(k) ORPHAN DRUGS.—A drug designated under section 526 for a rare disease or condition and approved under section 505 or under section 351 of the Public Health Service Act shall be exempt from product and facility fees under this section, provided that the drug meets all of the following:

(1) The drug had United States sales in the previous year of less than $25,000,000 for the active moiety, for all indications, dosage forms, and strengths for which the drug is approved and for any off-label uses.

(2) The drug meets the public health requirements contained in this Act as such requirements are applied to requests for waivers for product and facility fees.

(3) The drug is owned or licensed and marketed by a company that had less than $100,000,000 in gross worldwide revenue during the previous year.

SEC. 736A. FEES RELATING TO ADVISORY REVIEW OF PRESCRIPTION-DRUG TELEVISION ADVERTISING.

(a) TYPES OF DIRECT-TO-CONSUMER TELEVISION ADVERTISEMENT REVIEW FEES.—Beginning in fiscal year 2008, the Secretary shall assess and collect fees in accordance with this section as follows:

(1) ADVISORY REVIEW FEE.—

(A) IN GENERAL.—With respect to a proposed direct-to-consumer television advertisement (referred to in this section as a "DTC advertisement"), each person that on or after October 1, 2007, submits such an advertisement for advisory review by the Secretary prior to its initial public broadcast (referred to in this section as "prebroadcast advisory review") shall, except as provided in subparagraph (B), be subject to a fee established under subsection (c)(3).

(B) EXCEPTION FOR REQUIRED SUBMISSIONS.—A DTC advertisement that is required under section 502(n) to be submitted to the Secretary prior to initial public broadcast is not subject to a fee under subparagraph (A) unless the sponsor designates the submission as a submission for prebroadcast advisory review.

(C) NOTICE TO SECRETARY OF NUMBER OF ADVERTISEMENTS.—Not later than June 1 of each fiscal year, the Secretary shall publish a notice in the Federal Register requesting any person to notify the Secretary within 30 days of the number of DTC advertisements the person intends to submit for prebroadcast advisory review in the next fiscal year.

(D) PAYMENT.—

(i) IN GENERAL.—The fee required by subparagraph (A) (referred to in this section as "an advisory review fee") shall be due not later than October 1 of the fiscal year in which the DTC advertisement involved is intended be submitted for prebroadcast advisory review, subject to subparagraph (F)(i).

(ii) EFFECT OF SUBMISSION.—Notification of the Secretary under subparagraph (C) of the number of DTC advertisements a person intends to submit for prebroadcast advisory review is a legally binding commitment by that person to pay the annual advisory review fee for that number of submissions on or before October 1 of the fiscal year in which the advertisement is intended to be submitted.

(iii) NOTICE REGARDING CARRYOVER SUBMISSIONS.—In making a notification under subparagraph (C), the person involved shall in addition notify the Secretary if under subparagraph (F)(i) the person intends to submit a DTC advertisement for which the advisory review fee has already been paid. If the person does not so notify the Secretary, each DTC advertisement submitted

by the person for prebroadcast advisory review in the fiscal year involved shall be subject to the advisory review fee.

(E) MODIFICATION OF ADVISORY REVIEW FEE.—

(i) LATE PAYMENT.—If a person has submitted a notification under subparagraph (C) with respect to a fiscal year and has not paid all advisory review fees due under subparagraph (D) on or before November 1 of such fiscal year, the fees are regarded as late and a revised due date and an increase in the amount of fees applies in accordance with this clause, notwithstanding any other provision of this section. For such person, the advisory review fee for each DTC advertisement submitted in such fiscal year for prebroadcast advisory review shall be due and payable 20 days before the advertisement is submitted to the Secretary, and each such fee shall be revised to be equal to 150 percent of the fee that otherwise would have applied pursuant to subsection (c)(3).

(ii) EXCEEDING IDENTIFIED NUMBER OF SUBMISSIONS.—If a person submits a number of DTC ads for prebroadcast advisory review in a fiscal year that exceeds the number identified by the person under subparagraph (C), a revised due date and an increase in the amount of fees applies under this clause for each submission in excess of such number, notwithstanding any other provision of this section. For each such DTC ad, the advisory review fee shall be due and payable 20 days before the advertisement is submitted to the Secretary, and the fee shall be revised to be equal to 150 percent of the fee that otherwise would have applied pursuant to subsection (c)(3).

(F) LIMITS.—

(i) SUBMISSIONS.—For each advisory review fee paid by a person for a fiscal year, the person is entitled to acceptance for advisory review by the Secretary of one DTC advertisement and acceptance of one resubmission for advisory review of the same advertisement. The advertisement shall be submitted for review in the fiscal year for which the fee was assessed, except that a person may carry over not more than one paid advisory review submission to the next fiscal year. Resubmissions may be submitted without regard to the fiscal year of the initial advisory review submission.

(ii) NO REFUNDS.—Except as provided by subsection (f), fees paid under subparagraph (A) shall not be refunded.

(iii) NO WAIVERS, EXEMPTIONS, OR REDUCTIONS.—The Secretary shall not grant a waiver, exemption, or reduction of any fees due or payable under this section.

(iv) RIGHT TO ADVISORY REVIEW NOT TRANSFERABLE.—The right to an advisory review under this paragraph is not transferable, except to a successor in interest.

(2) OPERATING RESERVE FEE.—

(A) IN GENERAL.—Each person that on or after October 1, 2007, is assessed an advisory review fee under paragraph (1) shall be subject to fee established under subsection (d)(2) referred to in this section as an "operating reserve fee" for the first fiscal year in which an advisory review fee is assessed to such person. The person is not subject to an operating reserve fee for any other fiscal year.

(B) PAYMENT.—Except as provided in subparagraph (C), the operating reserve fee shall be due no later than October 1 of the first fiscal year in which the person is required to pay an advisory review fee under paragraph (1).

(C) LATE NOTICE OF SUBMISSION.—If, in the first fiscal year of a person's participation in the program under this section, that person submits any DTC advertisements for prebroadcast advisory review that are in excess of the number identified by that person in response to the Federal Register notice described in subsection (a)(1)(C), that person shall pay an operating reserve fee for each of those advisory reviews equal to the advisory review fee for each submission established under paragraph (1)(D)(ii). Fees required by this subparagraph shall be in addition to any fees required by subparagraph (A). Fees under this subparagraph shall be due 20 days before any DTC advertisement is submitted by such person to the Secretary for prebroadcast advisory review.

(b) ADVISORY REVIEW FEE REVENUE AMOUNTS.—Fees under subsection (a)(1) shall be established to generate revenue amounts of $6,250,000 for each of fiscal years 2008 through 2012, as adjusted pursuant to subsections (c) and (g)(4).

(c) ADJUSTMENTS.—

(1) INFLATION ADJUSTMENT.—Beginning with fiscal year 2009, the revenues established in subsection (b) shall be adjusted by the Secretary by notice, published in the Federal Register, for a fiscal year to reflect the greater of—

(A) the total percentage change that occurred in the Consumer Price Index for all urban consumers (all items; U.S. city average), for the 12-month period ending June 30 preceding the fiscal year for which fees are being established;

(B) the total percentage change for the previous fiscal year in basic pay under the General Schedule in accordance with section 5332 of title 5, United States Code, as adjusted by any locality-based comparability payment pursuant to section 5304 of such title for Federal employees stationed in the District of Columbia; or

(C) the average annual change in the cost, per full-time equivalent position of the Food and Drug Administration, of all personnel compensation and benefits paid with respect to such positions for the first 5 fiscal years of the previous 6 fiscal years.

The adjustment made each fiscal year by this subsection will be added on a compounded basis to the sum of all adjustments made each fiscal year after fiscal year 2008 under this subsection.

(2) WORKLOAD ADJUSTMENT.—Beginning with fiscal year 2009, after the fee revenues established in subsection (b) are ad-

justed for a fiscal year for inflation in accordance with paragraph (1), the fee revenues shall be adjusted further for such fiscal year to reflect changes in the workload of the Secretary with respect to the submission of DTC advertisements for advisory review prior to initial broadcast. With respect to such adjustment:

(A) The adjustment shall be determined by the Secretary based upon the number of DTC advertisements identified pursuant to subsection (a)(1)(C) for the upcoming fiscal year, excluding allowable previously paid carry over submissions. The adjustment shall be determined by multiplying the number of such advertisements projected for that fiscal year that exceeds 150 by $27,600 (adjusted each year beginning with fiscal year 2009 for inflation in accordance with paragraph (1)). The Secretary shall publish in the Federal Register the fee revenues and fees resulting from the adjustment and the supporting methodologies.

(B) Under no circumstances shall the adjustment result in fee revenues for a fiscal year that are less than the fee revenues established for the prior fiscal year.

(3) ANNUAL FEE SETTING FOR ADVISORY REVIEW.—

(A) IN GENERAL.—Not later than August 1 of each fiscal year, the Secretary shall establish for the next fiscal year the DTC advertisement advisory review fee under subsection (a)(1), based on the revenue amounts established under subsection (b), the adjustments provided under paragraphs (1) and (2), and the number of DTC advertisements identified pursuant to subsection (a)(1)(C), excluding allowable previously-paid carry over submissions. The annual advisory review fee shall be established by dividing the fee revenue for a fiscal year (as adjusted pursuant to this subsection) by the number of DTC advertisements so identified, excluding allowable previously-paid carry over submissions.

(B) FISCAL YEAR 2008 FEE LIMIT.—Notwithstanding subsection (b) and the adjustments pursuant to this subsection, the fee established under subparagraph (A) for fiscal year 2008 may not be more than $83,000 per submission for advisory review.

(C) ANNUAL FEE LIMIT.—Notwithstanding subsection (b) and the adjustments pursuant to this subsection, the fee established under subparagraph (A) for a fiscal year after fiscal year 2008 may not be more than 50 percent more than the fee established for the prior fiscal year.

(D) LIMIT.—The total amount of fees obligated for a fiscal year may not exceed the total costs for such fiscal year for the resources allocated for the process for the advisory review of prescription drug advertising.

(d) OPERATING RESERVES.—

(1) IN GENERAL.—The Secretary shall establish in the Food and Drug Administration salaries and expenses appropriation account without fiscal year limitation a Direct-to-Consumer Advisory Review Operating Reserve, of at least $6,250,000 in fiscal year 2008, to continue the program under this section in the event the fees collected in any subsequent fiscal year pursuant

to subsection (a)(1) do not generate the fee revenue amount established for that fiscal year.

(2) FEE SETTING.—The Secretary shall establish the operating reserve fee under subsection (a)(2)(A) for each person required to pay the fee by multiplying the number of DTC advertisements identified by that person pursuant to subsection (a)(1)(C) by the advisory review fee established pursuant to subsection (c)(3) for that fiscal year, except that in no case shall the operating reserve fee assessed be less than the operating reserve fee assessed if the person had first participated in the program under this section in fiscal year 2008.

(3) USE OF OPERATING RESERVE.—The Secretary may use funds from the reserves only to the extent necessary in any fiscal year to make up the difference between the fee revenue amount established for that fiscal year under subsections (b) and (c) and the amount of fees actually collected for that fiscal year pursuant to subsection (a)(1), or to pay costs of ending the program under this section if it is terminated pursuant to subsection (f) or not reauthorized beyond fiscal year 2012.

(4) REFUND OF OPERATING RESERVES.—Within 120 days of the end of fiscal year 2012, or if the program under this section ends early pursuant to subsection (f), the Secretary, after setting aside sufficient operating reserve amounts to terminate the program under this section, shall refund all amounts remaining in the operating reserve on a pro rata basis to each person that paid an operating reserve fee assessment. In no event shall the refund to any person exceed the total amount of operating reserve fees paid by such person pursuant to subsection (a)(2).

(e) EFFECT OF FAILURE TO PAY FEES.—Notwithstanding any other requirement, a submission for prebroadcast advisory review of a DTC advertisement submitted by a person subject to fees under subsection (a) shall be considered incomplete and shall not be accepted for review by the Secretary until all fees owed by such person under this section have been paid.

(f) EFFECT OF INADEQUATE FUNDING OF PROGRAM.—

(1) INITIAL FUNDING.—If on November 1, 2007, or 120 days after enactment of this provision, whichever is later, the Secretary has not received at least $11,250,000 in advisory review fees and operating reserve fees combined, the program under this section shall not commence and all collected fees shall be refunded.

(2) LATER FISCAL YEARS.—Beginning in fiscal year 2009, if, on November 1 of the fiscal year, the combination of the operating reserves, annual fee revenues from that fiscal year, and unobligated fee revenues from prior fiscal years falls below $9,000,000, adjusted for inflation (as described in subsection (c)(1)), the program under this section shall cease to exist, and the Secretary shall notify all participants, retain any money from the unused advisory review fees and the operating reserves needed to close down the program under this section, and refund the remainder of the unused fees and operating reserves. To the extent required to close down the program under this section, the Secretary shall first use unobligated advisory review fee revenues from prior fiscal years, then the operating re-

serves, and finally, unused advisory review fees from the relevant fiscal year.

(g) CREDITING AND AVAILABILITY OF FEES.—

(1) IN GENERAL.—Fees authorized under subsection (a) of this section shall be collected and available for obligation only to the extent and in the amount provided in advance in appropriations Acts. Such fees are authorized to remain available until expended. Such sums as may be necessary may be transferred from the Food and Drug Administration salaries and expenses appropriation account without fiscal year limitation to such appropriation account for salaries and expenses with such fiscal year limitation. The sums transferred shall be available solely for the process for the advisory review of prescription drug advertising.

(2) COLLECTIONS AND APPROPRIATION ACTS.—

(A) IN GENERAL.—The fees authorized by this section—

(i) shall be retained in each fiscal year in an amount not to exceed the amount specified in appropriation Acts, or otherwise made available for obligation for such fiscal year; and

(ii) shall be available for obligation only if the amounts appropriated as budget authority for such fiscal year are sufficient to support a number of full-time equivalent review employees that is not fewer than the number of such employees supported in fiscal year 2007.

(B) REVIEW EMPLOYEES.—For purposes of subparagraph (A)(ii), the term "full-time equivalent review employees" means the total combined number of full-time equivalent employees in—

(i) the Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, Food and Drug Administration; and

(ii) the Center for Biologics Evaluation and Research, Advertising and Promotional Labeling Branch, Food and Drug Administration.

(3) AUTHORIZATION OF APPROPRIATIONS.—For each of the fiscal years 2008 through 2012, there is authorized to be appropriated for fees under this section an amount equal to the total revenue amount determined under subsection (b) for the fiscal year, as adjusted pursuant to subsection (c) and paragraph (4) of this subsection, plus amounts collected for the reserve fund under subsection (d).

(4) OFFSET.—Any amount of fees collected for a fiscal year under this section that exceeds the amount of fees specified in appropriation Acts for such fiscal year shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be collected under this section pursuant to appropriation Acts for a subsequent fiscal year.

(h) DEFINITIONS.—For purposes of this subchapter:

(1) The term "advisory review" means reviewing and providing advisory comments on a proposed advertisement prior to its initial public broadcast.

(2) The term "advisory review fee" has the meaning indicated for such term in subsection (a)(1)(D).

(3) The term "carry over submission" means a submission for an advisory review for which a fee was paid in one fiscal year that is submitted for review in the following fiscal year.

(4) The term "direct-to-consumer television advertisement" means an advertisement for a prescription drug product as defined in section 735(3) intended to be displayed on any television channel for less than 3 minutes.

(5) The term "DTC advertisement" has the meaning indicated for such term in subsection (a)(1)(A).

(6) The term "operating reserve fee" has the meaning indicated for such term in subsection (a)(2)(A).

(7) The term "person" includes an individual, partnership, corporation, and association, and any affiliate thereof or successor in interest.

(8) The term "prebroadcast advisory review" has the meaning indicated for such term in subsection (a)(1)(A).

(9) The term "process for the advisory review of prescription drug advertising" means the activities necessary to review and provide advisory comments on DTC advertisements prior to public broadcast and, to the extent the Secretary has additional staff resources available under the program under this section that are not necessary for the advisory review of DTC advertisements, the activities necessary to review and provide advisory comments on other proposed advertisements and promotional material prior to public broadcast.

(10) The term "resources allocated for the process for the advisory review of prescription drug advertising" means the expenses incurred in connection with the process for the advisory review of prescription drug advertising for—

(A) officers and employees of the Food and Drug Administration, contractors of the Food and Drug Administration, advisory committees, and costs related to such officers, employees, and committees, and to contracts with such contractors;

(B) management of information, and the acquisition, maintenance, and repair of computer resources;

(C) leasing, maintenance, renovation, and repair of facilities and acquisition, maintenance, and repair of fixtures, furniture, scientific equipment, and other necessary materials and supplies;

(D) collection of fees under this section and accounting for resources allocated for the advisory review of prescription drug advertising; and

(E) closing down the program under this section pursuant to subsection (f)(2) if that becomes necessary.

(11) The term "resubmission" means a subsequent submission for advisory review of a direct-to-consumer television advertisement that has been revised in response to the Secretary's comments on an original submission. A resubmission may not introduce significant new concepts or creative themes into the television advertisement.

(12) The term "submission for advisory review" means an original submission of a direct-to-consumer television advertise-

ment for which the sponsor voluntarily requests advisory comments before the advertisement is publicly disseminated.

PART 3—FEES RELATING TO DEVICES

SEC. 737. DEFINITIONS.

For purposes of this subchapter:

(1) * * *

* * * * * * *

(4)(A) The term "supplement", with respect to a panel-track supplement, a 180-day supplement, a real-time supplement, [or an efficacy supplement,] *an efficacy supplement, or a 30-day notice,* means a request to the Secretary to approve a change in a device for which—

(i) * * *

* * * * * * *

(F) The term "30-day notice" means a supplement to an approved premarket application or premarket report under section 515 that is limited to a request to make modifications to manufacturing procedures or methods of manufacture affecting the safety and effectiveness of the device.

(5) The term "request for classification information" means a request made under section 513(g) for information respecting the class in which a device has been classified or the requirements applicable to a device.

(6) The term "annual fee", with respect to periodic reporting concerning a class III device, means the annual fee associated with periodic reports required by a PMA approval order (as described in section 814.82(a)(7) of title 21, Code of Federal Regulations (or any successor regulation)).

[(5)] *(7)* The term "process for the review of device applications" means the following activities of the Secretary with respect to the review of premarket applications, premarket reports, supplements, and premarket notification submissions:

(A) * * *

* * * * * * *

[(6)] *(8)* The term "costs of resources allocated for the process for the review of device applications" means the expenses incurred in connection with the process for the review of device applications for—

(A) * * *

* * * * * * *

[(7)] *(9)* The term "adjustment factor" applicable to a fiscal year is the Consumer Price Index for all urban consumers (all items; United States city average) for [April of the preceding fiscal year] *October of the preceding fiscal year* divided by such Index for [April 2002] *October 2001.*

(10) The term "person" includes an affiliate thereof.

[(8)] *(11)* The term "affiliate" means a business entity that has a relationship with a second business entity (whether domestic or international) if, directly or indirectly—

(A)

* * * * * * *

(12) The term "establishment subject to registration" means an establishment that is required to register with the Secretary under section 510 and is one of the following types of establishments:

(A) MANUFACTURER.—An establishment that makes by any means any article that is a device, as defined in section 201(h), including an establishment that sterilizes or otherwise makes such article for or on behalf of a specification developer or any other person.

(B) SINGLE-USE DEVICE REPROCESSOR.—An establishment that performs manufacturing operations on a single-use device.

(C) SPECIFICATION DEVELOPER.—An establishment that develops specifications for a device that is distributed under the establishment's name but which performs no manufacturing, including an establishment that, in addition to developing specifications, also arranges for the manufacturing of devices labeled with another establishment's name by a contract manufacturer.

SEC. 738. AUTHORITY TO ASSESS AND USE DEVICE FEES.

(a) TYPES OF FEES.—

(1) * * *

(2) [PREMARKET APPLICATION, PREMARKET REPORT, SUPPLEMENT, AND SUBMISSION FEE] *PREMARKET APPLICATION, PREMARKET REPORT, SUPPLEMENT, AND SUBMISSION FEE, AND ANNUAL FEE FOR PERIODIC REPORTING CONCERNING A CLASS III DEVICE.*—

(A) IN GENERAL.—Except as provided in subparagraph (B) and subsections (d) and (e), each person who submits any of the following, on or after October 1, 2002, shall be subject to a fee established under subsection (c)(1) for the fiscal year involved in accordance with the following:

(i) * * *

* * * * * * *

(iii) For a panel track supplement, [a fee equal to the fee that applies] *a fee equal to 75 percent of the fee that applies* under clause (i).

(iv) For a 180-day supplement, a fee equal to [21.5 percent] *15 percent* of the fee that applies under clause (i).

(v) For a real-time supplement, a fee equal to [7.2 percent] *7 percent* of the fee that applies under clause (i).

(vi) For a 30-day notice, a fee equal to 1.6 percent of the fee that applies under clause (i).

[(vi)] *(vii)* For an efficacy supplement, a fee equal to the fee that applies under clause (i).

[(vii)] *(viii)* For a premarket notification submission, a fee equal to [1.42 percent] *1.84 percent* of the fee that applies under clause (i), subject to any adjustment under subsection (e)(2)(C)(ii).

(ix) For a request for classification information, a fee equal to 1.35 percent of the fee that applies under clause (i).

(x) For periodic reporting concerning a class III device, the annual fee shall be equal to 3.5 percent of the fee that applies under clause (i).

* * * * * * *

[(C) PAYMENT.—The fee required by subparagraph (A) shall be due upon submission of the premarket application, premarket report, supplement, or premarket notification submission except that invoices for applications submitted between October 1, 2002, and the date of the enactment of the Medical Device User Fee and Modernization Act of 2002 shall be payable on October 30, 2002. Applicants submitting portions of applications pursuant to section 515(c)(3) shall pay such fees upon submission of the first portion of such applications. The fees credited to fiscal year 2003 under this section shall include all fees payable from October 1, 2002, through September 30, 2003.]

(C) PAYMENT.—The fee required by subparagraph (A) shall be due upon submission of the premarket application, premarket report, supplement, premarket notification submission, 30-day notice, request for classification information, or periodic reporting concerning a class III device. Applicants submitting portions of applications pursuant to section 515(c)(3) shall pay such fees upon submission of the first portion of such applications.

(D) REFUNDS.—

(i) * * *

* * * * * * *

(iv) MODULAR APPLICATIONS WITHDRAWN BEFORE FIRST ACTION.—The Secretary shall refund 75 percent of the application fee paid for a modular application submitted under section 515(c)(4) that is withdrawn before a second module is submitted and before a first action on the first module. If the modular application is withdrawn after a second or subsequent module is submitted but before any first action, the Secretary may return a portion of the fee. The amount of refund, if any, shall be based on the level of effort already expended on the review of the modules submitted.

(3) ANNUAL ESTABLISHMENT REGISTRATION FEE.—

(A) IN GENERAL.—Except as provided in subparagraph (B), each establishment subject to registration shall be subject to a fee for each initial or annual registration under section 510 beginning with its registration for fiscal year 2008.

(B) EXCEPTION.—No fee shall be required under subparagraph (A) for an establishment operated by a State or Federal governmental entity or an Indian tribe (as defined in the Indian Self Determination and Educational Assistance Act), unless a device manufactured by the establishment is to be distributed commercially.

(C) PAYMENT.—The fee required under subparagraph (A) shall be due once each fiscal year, upon the initial registration of the establishment or upon the annual registration under section 510.

[(b) FEE REVENUE AMOUNTS.—Except as provided in subsections (c), (d), (e), (g), and (h), the fees under subsection (a) shall be established to generate the following revenue amounts: $25,125,000 in fiscal year 2003; $27,255,000 in fiscal year 2004; and $29,785,000 in fiscal year 2005. If legislation is enacted after the date of the enactment of the Medical Device User Fee and Modernization Act of 2002 requiring the Secretary to fund additional costs of the retirement of Federal personnel, fee revenue amounts under this subsection shall be increased in each year by the amount necessary to fully fund the portion of such additional costs that are attributable to the process for the review of device applications.]

(b) FEE AMOUNTS.—Except as provided in subsections (c), (d), and (e), the fees under subsection (a) shall be based on the following fee amounts:

Fee Type	*Fiscal Year 2008*	*Fiscal Year 2009*	*Fiscal Year 2010*	*Fiscal Year 2011*	*Fiscal Year 2012*
Premarket Application	*$185,000*	*$200,725*	*$217,787*	*$236,298*	*$256,384*
Establishment Registration	*$1,706*	*$1,851*	*$2,008*	*$2,179*	*$2,364.*

(c) [Annual Fee Setting] *ANNUAL FEE SETTING.—*

(1) IN GENERAL.—The Secretary shall, 60 days before the start of each fiscal year after September 30, 2002, publish in the Federal Register fees under subsection (a). [The fees established for fiscal year 2006 shall be based on a premarket application fee of $259,600, and the fees established for fiscal year 2007 shall be based on a premarket application fee of $281,600.]

(2) ADJUSTMENT.—

(A) IN GENERAL.—When setting fees for fiscal year 2010, the Secretary may increase the fee under subsection (a)(3)(A) (applicable to establishments subject to registration) only if the Secretary estimates that the number of establishments submitting fees for fiscal year 2009 is less than 12,250. The percentage increase shall be the percentage by which the estimate of establishments submitting fees in fiscal year 2009 is less than 12,750, but in no case may the percentage increase be more than 8.5 percent over that specified in subsection (b) for fiscal year 2010. If the Secretary makes any adjustment to the fee under subsection (a)(3)(A) for fiscal year 2010, then such fee for fiscal years 2011 and 2012 shall be adjusted so that such fee for fiscal year 2011 is equal to the adjusted fee for fiscal year 2010 increased by 8.5 percent, and such fee for fiscal year 2012 is equal to the adjusted fee for fiscal year 2011 increased by 8.5 percent.

(B) PUBLICATION.—For any adjustment made under subparagraph (A), the Secretary shall publish in the Federal

Register the Secretary's determination to make the adjustment and the rationale for the determination.

[(2)] *(3)* LIMIT.—The total amount of fees charged, as adjusted under this subsection, for a fiscal year may not exceed the total costs for such fiscal year for the resources allocated for the process for the review of device applications.

[(3)] *(4)* SUPPLEMENT.—

(A) IN GENERAL.—[For fiscal years 2006 and 2007, the Secretary] *The Secretary* may use unobligated carryover balances from fees collected in previous fiscal years to ensure that sufficient fee revenues are available in that fiscal year, so long as the Secretary maintains unobligated carryover balances of not less than 1 month of operating reserves [for the first month of fiscal year 2008] *for the first month of the next fiscal year*.

* * * * * * *

(d) SMALL BUSINESSES; FEE WAIVER AND FEE REDUCTION REGARDING PREMARKET APPROVAL FEES.—

(1) IN GENERAL.—The Secretary shall grant a waiver of the fee required under subsection (a) for one premarket application, or one premarket report, where the Secretary finds that the applicant involved is a small business submitting its first premarket application to the Secretary, or its first premarket report, respectively, for review. For the purposes of this paragraph, the term "small business" means an entity that reported $30,000,000 or less of gross receipts or sales in its most recent Federal income tax return for a taxable year, including such returns of all of its affiliates[, partners, and parent firms]. In addition, for subsequent premarket applications, premarket reports, and supplements where the Secretary finds that the applicant involved is a small business, the fees specified in [clauses (i) through (vi) of subsection (a)(2)(A)] *clauses (i) through (v) and clauses (vii), (ix), and (x) of subsection (a)(2)(A)* may be paid at a reduced rate in accordance with paragraph (2)(C).

(2) RULES RELATING TO PREMARKET APPROVAL FEES.—

(A) DEFINITION.—For purposes of this paragraph, the term "small business" means an entity that reported $100,000,000 or less of gross receipts or sales in its most recent Federal income tax return for a taxable year, including such returns of all of its affiliates[, partners, and parent firms].

[(B) EVIDENCE OF QUALIFICATION.—An applicant]

(B) EVIDENCE OF QUALIFICATION.—

(i) IN GENERAL.—An applicant shall pay the higher fees established by the Secretary each year unless the applicant submits evidence that it qualifies for a waiver of the fee or the lower fee rate. [The applicant shall support its claim]

(ii) FIRMS SUBMITTING TAX RETURNS TO THE UNITED STATES INTERNAL REVENUE SERVICE.—The applicant shall support its claim that it meets the definition under subparagraph (A) by submission of a copy of its most recent Federal income tax return for a taxable year, and a copy of such returns of its affiliates[, part-

ners, and parent firms**]**, which show an amount of gross sales or receipts that is less than the maximum established in subparagraph (A). The applicant, and each of such affiliates**[**, partners, and parent firms**]**, shall certify that the information provided is a true and accurate copy of the actual tax forms they submitted to the Internal Revenue Service. **[**If no tax forms are submitted for affiliates, partners, or parent firms, the applicant shall certify that the applicant has no affiliates, partners, or parent firms, respectively.**]** *If no tax forms are submitted for any affiliate, the applicant shall certify that the applicant has no affiliates.*

(iii) FIRMS NOT SUBMITTING TAX RETURNS TO THE UNITED STATES INTERNAL REVENUE SERVICE.—In the case of an applicant that has not previously submitted a Federal income tax return, the applicant and each of its affiliates shall demonstrate that it meets the definition under subparagraph (A) by submission of a signed certification, in such form as the Secretary may direct through a notice published in the Federal Register, that the applicant or affiliate meets the criteria for a small business and a certification, in English, from the national taxing authority of the country in which the applicant or, if applicable, affiliate is headquartered. The certification from such taxing authority shall bear the official seal of such taxing authority and shall provide the applicant's or affiliate's gross receipts and sales for the most recent year in both the local currency of such country and in United States dollars, the exchange rate used in converting such local currency to dollars, and the dates during which these receipts and sales were collected. The applicant shall also submit a statement signed by the head of the applicant's firm or by its chief financial officer that the applicant has submitted certifications for all of its affiliates, or that the applicant has no affiliates.

[(C) REDUCED FEES.—Where the Secretary finds that the applicant involved meets the definition under subparagraph (A), the fees established under subsection (c)(1) may be paid at a reduced rate of 38 percent of the fee established under such subsection for a premarket application, a premarket report, or a supplement.**]**

(C) REDUCED FEES.—Where the Secretary finds that the applicant involved meets the definition under subparagraph (A), the fees established under subsection (c)(1) may be paid at a reduced rate of—

(i) 25 percent of the fee established under such subsection for a premarket application, a premarket report, a supplement (other than a 30-day notice), or periodic reporting concerning a class III device; and

(ii) 50 percent of the fee established under such subsection for a 30-day notice or a request for classification information.

* * * * * * *

(e) SMALL BUSINESSES; FEE REDUCTION REGARDING PREMARKET NOTIFICATION SUBMISSIONS.—

(1) IN GENERAL.—For fiscal year [2004] *2008* and each subsequent fiscal year, where the Secretary finds that the applicant involved is a small business, the fee specified in subsection [(a)(2)(A)(vii)] *(a)(2)(A)(viii)* may be paid at a reduced rate in accordance with paragraph (2)(C).

(2) RULES RELATING TO PREMARKET NOTIFICATION SUBMISSIONS.—

(A) DEFINITION.—For purposes of this subsection, the term "small business" means an entity that reported $100,000,000 or less of gross receipts or sales in its most recent Federal income tax return for a taxable year, including such returns of all of its affiliates[, partners, and parent firms].

(B) EVIDENCE OF QUALIFICATION.—

(i) IN GENERAL.—An applicant shall pay the higher fees established by the Secretary each year unless the applicant submits evidence that it qualifies for the lower fee rate. [The applicant shall support its claim]

(ii) FIRMS SUBMITTING TAX RETURNS TO THE UNITED STATES INTERNAL REVENUE SERVICE.—The applicant shall support its claim that it meets the definition under subparagraph (A) by submission of a copy of its most recent Federal income tax return for a taxable year, and a copy of such returns of its affiliates[, partners, and parent firms], which show an amount of gross sales or receipts that is less than the maximum established in subparagraph (A). The applicant, and each of such affiliates[, partners, and parent firms], shall certify that the information provided is a true and accurate copy of the actual tax forms they submitted to the Internal Revenue Service. [If no tax forms are submitted for affiliates, partners, or parent firms, the applicant shall certify that the applicant has no affiliates, partners, or parent firms, respectively.] *If no tax forms are submitted for any affiliate, the applicant shall certify that the applicant has no affiliates.*

(iii) FIRMS NOT SUBMITTING TAX RETURNS TO THE UNITED STATES INTERNAL REVENUE SERVICE.—In the case of an applicant that has not previously submitted a Federal income tax return, the applicant and each of its affiliates shall demonstrate that it meets the definition under subparagraph (A) by submission of a signed certification, in such form as the Secretary may direct through a notice published in the Federal Register, that the applicant or affiliate meets the criteria for a small business and a certification, in English, from the national taxing authority of the country in which the applicant or, if applicable, affiliate is headquartered. The certification from such taxing authority shall bear the official seal of such taxing authority and shall provide the applicant's or affiliate's gross receipts and sales for the most recent year in both the local currency

of such country and in United States dollars, the exchange rate used in converting such local currency to dollars, and the dates during which these receipts and sales were collected. The applicant shall also submit a statement signed by the head of the applicant's firm or by its chief financial officer that the applicant has submitted certifications for all of its affiliates, or that the applicant has no affiliates.

[(C) REDUCED FEES.—

[(i) IN GENERAL.—For fiscal year 2004 and each subsequent fiscal year, where the Secretary finds that the applicant involved meets the definition under subparagraph (A), the fee for a premarket notification submission may be paid at 80 percent of the fee that applies under subsection (a)(2)(A)(vii), as adjusted under clause (ii) and as established under subsection (c)(1).

[(ii) ADJUSTMENT PER FEE REVENUE AMOUNT.—For fiscal year 2004 and each subsequent fiscal year, the Secretary, in setting the revenue amount under subsection (c)(1) for premarket notification submissions, shall determine the revenue amount that would apply if all such submissions for the fiscal year involved paid a fee equal to 1.42 percent of the amount that applies under subsection (a)(2)(A)(i) for premarket applications, and shall adjust the fee under subsection (a)(2)(A)(vii) for premarket notification submissions such that the reduced fees collected under clause (i) of this subparagraph, when added to fees for such submissions that are not paid at the reduced rate, will equal such revenue amount for the fiscal year.]

(C) REDUCED FEES.—For fiscal year 2008 and each subsequent fiscal year, where the Secretary finds that the applicant involved meets the definition under subparagraph (A), the fee for a premarket notification submission may be paid at 50 percent of the fee that applies under subsection (a)(2)(A)(viii), and as established under subsection (c)(1).

* * * * * * *

[(f) EFFECT OF FAILURE TO PAY FEES.—A premarket application, premarket report, supplement, or premarket notification submission submitted by a person subject to fees under subsection (a) shall be considered incomplete and shall not be accepted by the Secretary until all fees owed by such person have been paid.]

(f) EFFECT OF FAILURE TO PAY FEES.—

(1) NO ACCEPTANCE OF SUBMISSIONS.—A premarket application, premarket report, supplement, premarket notification submission, 30-day notice, request for classification information, or periodic reporting concerning a class III device submitted by a person subject to fees under subsection (a)(2) and (a)(3) shall be considered incomplete and shall not be accepted by the Secretary until all fees owed by such person have been paid.

(2) NO REGISTRATION.—Registration information submitted under section 510 by an establishment subject to registration shall be considered incomplete and shall not be accepted by the Secretary until the registration fee under subsection (a)(3) owed for the establishment has been paid. Until the fee is paid and

the registration is complete, the establishment is deemed to have failed to register in accordance with section 510.

(g) CONDITIONS.—

(1) PERFORMANCE GOALS THROUGH FISCAL YEAR 2005; TERMINATION OF PROGRAM AFTER FISCAL YEAR 2005.—With respect to the amount that, under the salaries and expenses account of the Food and Drug Administration, is appropriated for a fiscal year for devices and radiological products:

(A) * * *

* * * * * * *

(D) ⟦For fiscal year 2007⟧ *For fiscal year 2007 and for each subsequent year*, fees may not be assessed under subsection (a) for the fiscal year, and the Secretary is not expected to meet any performance goals identified for the fiscal year, if—

(i) the amount so appropriated for the fiscal year, excluding the amount of fees appropriated for the fiscal year, is more than 1 percent less than $205,720,000 multiplied by the adjustment factor ⟦applicable to fiscal year 2007⟧ *applicable to such fiscal year*; or

(ii) pursuant to ⟦subparagraph (C)⟧ *this subparagraph*, fees were not assessed under subsection (a) ⟦for fiscal year 2006⟧ *for the previous fiscal year*.

⟦(2) AUTHORITY.—If the Secretary does not assess fees under subsection (a) during any portion of a fiscal year because of subparagraph (C) or (D) of paragraph (1) and if at a later date in such fiscal year the Secretary may assess such fees, the Secretary may assess and collect such fees, without any modification in the rate for premarket applications, supplements, premarket reports, and premarket notification submissions, and at any time in such fiscal year, notwithstanding the provisions of subsection (a) relating to the date fees are to be paid.⟧

(2) AUTHORITY.—If the Secretary does not assess fees under subsection (a) during any portion of a fiscal year because of subparagraph (C) or (D) of paragraph (1) and if at a later date in such fiscal year the Secretary may assess such fees, the Secretary may assess and collect such fees, without any modification in the rate for premarket applications, supplements, premarket reports, premarket notification submissions, 30-day notices, requests for classification information, periodic reporting concerning a class III device, and establishment registrations at any time in such fiscal year, notwithstanding the provisions of subsection (a) relating to the date fees are to be paid.

(h) CREDITING AND AVAILABILITY OF FEES.—

(1) * * *

* * * * * * *

⟦(3) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated for fees under this section—

⟦(A) $25,125,000 for fiscal year 2003;

⟦(B) $27,255,000 for fiscal year 2004;

⟦(C) $29,785,000 for fiscal year 2005; and

⟦(D) such sums as may be necessary for each of fiscal years 2006 and 2007.

as adjusted to reflect adjustments in the total fee revenues made under this section and changes in the total amounts collected by application fees.

[(4) OFFSET.—Any amount of fees collected for a fiscal year under this section that exceeds the amount of fees specified in appropriation Acts for such fiscal year shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be authorized to be collected under this section pursuant to appropriation Acts for a subsequent fiscal year.]

(3) AUTHORIZATIONS OF APPROPRIATIONS.—There are authorized to be appropriated for fees under this section—

(A) $48,431,000 for fiscal year 2008;

(B) $52,547,000 for fiscal year 2009;

(C) $57,014,000 for fiscal year 2010;

(D) $61,860,000 for fiscal year 2011; and

(E) $67,118,000 for fiscal year 2012.

(4) OFFSET.—If the cumulative amount of fees collected during fiscal years 2008, 2009, and 2010, added to the amount estimated to be collected for fiscal year 2011, which estimate shall be based upon the amount of fees received by the Secretary through June 30, 2011, exceeds the amount of fees specified in aggregate in paragraph (3) for these four fiscal years, the aggregate amount in excess shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be authorized to be collected under this section pursuant to appropriation Acts for fiscal year 2012.

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SUBCHAPTER D—INFORMATION AND EDUCATION

* * * * * * *

SEC. 742. EDUCATION.

(a) * * *

(b) INTRAMURAL FELLOWSHIPS AND OTHER TRAINING PROGRAMS.—The Secretary, acting through the Commissioner, may, through fellowships and other training programs, conduct and support intramural research training for predoctoral and postdoctoral scientists and physicians. *Any such fellowships and training programs under this section or under section 770(d)(2)(A)(ix) may include provision by such scientists and physicians of services on a voluntary and uncompensated basis, as the Secretary determines appropriate. Such scientists and physicians shall be subject to all legal and ethical requirements otherwise applicable to officers or employees of the Department of Health and Human Services.*

* * * * * * *

Subchapter I—Reagan-Udall Foundation for the Food and Drug Administration

SEC. 770. ESTABLISHMENT AND FUNCTIONS OF THE FOUNDATION.

(a) IN GENERAL.—A nonprofit corporation to be known as the Reagan-Udall Foundation for the Food and Drug Administration

(referred to in this subchapter as the "Foundation") shall be established in accordance with this section. The Foundation shall be headed by an Executive Director, appointed by the members of the Board of Directors under subsection (e). The Foundation shall not be an agency or instrumentality of the United States Government.

(b) PURPOSE OF FOUNDATION.—The purpose of the Foundation is to advance the mission of the Food and Drug Administration to modernize medical, veterinary, food, food ingredient, and cosmetic product development, accelerate innovation, and enhance product safety.

(c) DUTIES OF THE FOUNDATION.—The Foundation shall—

(1) taking into consideration the Critical Path reports and priorities published by the Food and Drug Administration, identify unmet needs in the development, manufacture, and evaluation of the safety and effectiveness, including post-approval, of devices, including diagnostics, biologics, and drugs, and the safety of food, food ingredients, and cosmetics, and including the incorporation of more sensitive and predictive tools and devices to measure safety;

(2) establish goals and priorities in order to meet the unmet needs identified in paragraph (1);

(3) in consultation with the Secretary, identify existing and proposed Federal intramural and extramural research and development programs relating to the goals and priorities established under paragraph (2), coordinate Foundation activities with such programs, and minimize Foundation duplication of existing efforts;

(4) award grants to, or enter into contracts, memoranda of understanding, or cooperative agreements with, scientists and entities, which may include the Food and Drug Administration, university consortia, public-private partnerships, institutions of higher education, entities described in section 501(c)(3) of the Internal Revenue Code (and exempt from tax under section 501(a) of such Code), and industry, to efficiently and effectively advance the goals and priorities established under paragraph (2);

(5) recruit meeting participants and hold or sponsor (in whole or in part) meetings as appropriate to further the goals and priorities established under paragraph (2);

(6) release and publish information and data and, to the extent practicable, license, distribute, and release material, reagents, and techniques to maximize, promote, and coordinate the availability of such material, reagents, and techniques for use by the Food and Drug Administration, nonprofit organizations, and academic and industrial researchers to further the goals and priorities established under paragraph (2);

(7) ensure that—

(A) action is taken as necessary to obtain patents for inventions developed by the Foundation or with funds from the Foundation;

(B) action is taken as necessary to enable the licensing of inventions developed by the Foundation or with funds from the Foundation; and

(C) executed licenses, memoranda of understanding, material transfer agreements, contracts, and other such instru-

ments, promote, to the maximum extent practicable, the broadest conversion to commercial and noncommercial applications of licensed and patented inventions of the Foundation to further the goals and priorities established under paragraph (2);

(8) provide objective clinical and scientific information to the Food and Drug Administration and, upon request, to other Federal agencies to assist in agency determinations of how to ensure that regulatory policy accommodates scientific advances and meets the agency's public health mission;

(9) conduct annual assessments of the unmet needs identified in paragraph (1); and

(10) carry out such other activities consistent with the purposes of the Foundation as the Board determines appropriate.

(d) BOARD OF DIRECTORS.—

(1) ESTABLISHMENT.—

(A) IN GENERAL.—The Foundation shall have a Board of Directors (referred to in this subchapter as the "Board"), which shall be composed of ex officio and appointed members in accordance with this subsection. All appointed members of the Board shall be voting members.

(B) EX OFFICIO MEMBERS.—The ex officio members of the Board shall be the following individuals or their designees:

(i) The Commissioner.

(ii) The Director of the National Institutes of Health.

(iii) The Director of the Centers for Disease Control and Prevention.

(iv) The Director of the Agency for Healthcare Research and Quality.

(C) APPOINTED MEMBERS.—

(i) IN GENERAL.—The ex officio members of the Board under subparagraph (B) shall, by majority vote, appoint to the Board 12 individuals, from a list of candidates to be provided by the National Academy of Sciences. Of such appointed members—

(I) 4 shall be representatives of the general pharmaceutical, device, food, cosmetic, and biotechnology industries;

(II) 3 shall be representatives of academic research organizations;

(III) 2 shall be representatives of Government agencies, including the Food and Drug Administration and the National Institutes of Health;

(IV) 2 shall be representatives of patient or consumer advocacy organizations; and

(V) 1 shall be a representative of health care providers.

(ii) REQUIREMENT.—The ex officio members shall ensure the Board membership includes individuals with expertise in areas including the sciences of developing, manufacturing, and evaluating the safety and effectiveness of devices, including diagnostics, biologics, and drugs, and the safety of food, food ingredients, and cosmetics.

(D) INITIAL MEETING.—

(i) IN GENERAL.—Not later than 30 days after the date of the enactment of this Act, the Secretary shall convene a meeting of the ex officio members of the Board to—

(I) incorporate the Foundation; and

(II) appoint the members of the Board in accordance with subparagraph (C).

(ii) SERVICE OF EX OFFICIO MEMBERS.—Upon the appointment of the members of the Board under clause (i)(II), the terms of service of the ex officio members of the Board as members of the Board shall terminate.

(iii) CHAIR.—The ex officio members of the Board under subparagraph (B) shall designate an appointed member of the Board to serve as the Chair of the Board.

(2) DUTIES OF BOARD.—The Board shall—

(A) establish bylaws for the Foundation that—

(i) are published in the Federal Register and available for public comment;

(ii) establish policies for the selection of the officers, employees, agents, and contractors of the Foundation;

(iii) establish policies, including ethical standards, for the acceptance, solicitation, and disposition of donations and grants to the Foundation and for the disposition of the assets of the Foundation, including appropriate limits on the ability of donors to designate, by stipulation or restriction, the use or recipient of donated funds;

(iv) establish policies that would subject all employees, fellows, and trainees of the Foundation to the conflict of interest standards under section 208 of title 18, United States Code;

(v) establish licensing, distribution, and publication policies that support the widest and least restrictive use by the public of information and inventions developed by the Foundation or with Foundation funds to carry out the duties described in paragraphs (6) and (7) of subsection (c), and may include charging cost-based fees for published material produced by the Foundation;

(vi) specify principles for the review of proposals and awarding of grants and contracts that include peer review and that are consistent with those of the Foundation for the National Institutes of Health, to the extent determined practicable and appropriate by the Board;

(vii) specify a cap on administrative expenses for recipients of a grant, contract, or cooperative agreement from the Foundation;

(viii) establish policies for the execution of memoranda of understanding and cooperative agreements between the Foundation and other entities, including the Food and Drug Administration;

(ix) establish policies for funding training fellowships, whether at the Foundation, academic or scientific institutions, or the Food and Drug Administration, for scientists, doctors, and other professionals who are not employees of regulated industry, to foster great-

er understanding of and expertise in new scientific tools, diagnostics, manufacturing techniques, and potential barriers to translating basic research into clinical and regulatory practice;

(x) specify a process for annual Board review of the operations of the Foundation; and

(xi) establish specific duties of the Executive Director;

(B) prioritize and provide overall direction to the activities of the Foundation;

(C) evaluate the performance of the Executive Director; and

(D) carry out any other necessary activities regarding the functioning of the Foundation.

(3) TERMS AND VACANCIES.—

(A) TERM.—The term of office of each member of the Board appointed under paragraph (1)(C) shall be 4 years, except that the terms of offices for the initial appointed members of the Board shall expire on a staggered basis as determined by the ex officio members.

(B) VACANCY.—Any vacancy in the membership of the Board—

(i) shall not affect the power of the remaining members to execute the duties of the Board; and

(ii) shall be filled by appointment by the appointed members described in paragraph (1)(C) by majority vote.

(C) PARTIAL TERM.—If a member of the Board does not serve the full term applicable under subparagraph (A), the individual appointed under subparagraph (B) to fill the resulting vacancy shall be appointed for the remainder of the term of the predecessor of the individual.

(D) SERVING PAST TERM.—A member of the Board may continue to serve after the expiration of the term of the member until a successor is appointed.

(4) COMPENSATION.—Members of the Board may not receive compensation for service on the Board. Such members may be reimbursed for travel, subsistence, and other necessary expenses incurred in carrying out the duties of the Board, as set forth in the bylaws issued by the Board.

(e) INCORPORATION.—The ex officio members of the Board shall serve as incorporators and shall take whatever actions necessary to incorporate the Foundation.

(f) NONPROFIT STATUS.—The Foundation shall be considered to be a corporation under section 501(c) of the Internal Revenue Code of 1986, and shall be subject to the provisions of such section.

(g) EXECUTIVE DIRECTOR.—

(1) IN GENERAL.—The Board shall appoint an Executive Director who shall serve at the pleasure of the Board. The Executive Director shall be responsible for the day-to-day operations of the Foundation and shall have such specific duties and responsibilities as the Board shall prescribe.

(2) COMPENSATION.—The compensation of the Executive Director shall be fixed by the Board but shall not be greater than the compensation of the Commissioner.

(h) ADMINISTRATIVE POWERS.—In carrying out this subchapter, the Board, acting through the Executive Director, may—

(1) adopt, alter, and use a corporate seal, which shall be judicially noticed;

(2) hire, promote, compensate, and discharge 1 or more officers, employees, and agents, as may be necessary, and define their duties;

(3) prescribe the manner in which—

(A) real or personal property of the Foundation is acquired, held, and transferred;

(B) general operations of the Foundation are to be conducted; and

(C) the privileges granted to the Board by law are exercised and enjoyed;

(4) with the consent of the applicable executive department or independent agency, use the information, services, and facilities of such department or agencies in carrying out this section;

(5) enter into contracts with public and private organizations for the writing, editing, printing, and publishing of books and other material;

(6) hold, administer, invest, and spend any gift, devise, or bequest of real or personal property made to the Foundation under subsection (i);

(7) enter into such other contracts, leases, cooperative agreements, and other transactions as the Board considers appropriate to conduct the activities of the Foundation;

(8) modify or consent to the modification of any contract or agreement to which it is a party or in which it has an interest under this subchapter;

(9) take such action as may be necessary to obtain patents and licenses for devices and procedures developed by the Foundation and its employees;

(10) sue and be sued in its corporate name, and complain and defend in courts of competent jurisdiction;

(11) appoint other groups of advisors as may be determined necessary to carry out the functions of the Foundation; and

(12) exercise other powers as set forth in this section, and such other incidental powers as are necessary to carry out its powers, duties, and functions in accordance with this subchapter.

(i) ACCEPTANCE OF FUNDS FROM OTHER SOURCES.—The Executive Director may solicit and accept on behalf of the Foundation, any funds, gifts, grants, devises, or bequests of real or personal property made to the Foundation, including from private entities, for the purposes of carrying out the duties of the Foundation.

(j) SERVICE OF FEDERAL EMPLOYEES.—Federal Government employees may serve on committees advisory to the Foundation and otherwise cooperate with and assist the Foundation in carrying out its functions, so long as such employees do not direct or control Foundation activities.

(k) DETAIL OF GOVERNMENT EMPLOYEES; FELLOWSHIPS.—

(1) DETAIL FROM FEDERAL AGENCIES.—Federal Government employees may be detailed from Federal agencies with or without reimbursement to those agencies to the Foundation at any time, and such detail shall be without interruption or loss of

civil service status or privilege. Each such employee shall abide by the statutory, regulatory, ethical, and procedural standards applicable to the employees of the agency from which such employee is detailed and those of the Foundation.

(2) VOLUNTARY SERVICE; ACCEPTANCE OF FEDERAL EMPLOYEES.—

(A) FOUNDATION.—The Executive Director of the Foundation may accept the services of employees detailed from Federal agencies with or without reimbursement to those agencies.

(B) FOOD AND DRUG ADMINISTRATION.—The Commissioner may accept the uncompensated services of Foundation fellows or trainees. Such services shall be considered to be undertaking an activity under contract with the Secretary as described in section 708.

(l) ANNUAL REPORTS.—

(1) REPORTS TO FOUNDATION.—Any recipient of a grant, contract, fellowship, memorandum of understanding, or cooperative agreement from the Foundation under this section shall submit to the Foundation a report on an annual basis for the duration of such grant, contract, fellowship, memorandum of understanding, or cooperative agreement, that describes the activities carried out under such grant, contract, fellowship, memorandum of understanding, or cooperative agreement.

(2) REPORT TO CONGRESS AND THE FDA.—Beginning with fiscal year 2009, the Executive Director shall submit to Congress and the Commissioner an annual report that—

(A) describes the activities of the Foundation and the progress of the Foundation in furthering the goals and priorities established under subsection (c)(2), including the practical impact of the Foundation on regulated product development;

(B) provides a specific accounting of the source and use of all funds used by the Foundation to carry out such activities; and

(C) provides information on how the results of Foundation activities could be incorporated into the regulatory and product review activities of the Food and Drug Administration.

(m) SEPARATION OF FUNDS.—The Executive Director shall ensure that the funds received from the Treasury are held in separate accounts from funds received from entities under subsection (i).

(n) FUNDING.—From amounts appropriated to the Food and Drug Administration for each fiscal year, the Commissioner shall transfer not less than $500,000 and not more than $1,250,000, to the Foundation to carry out subsections (a), (b), and (d) through (m).

SEC. 771. LOCATION OF FOUNDATION.

The Foundation shall, if practicable, be located not more than 20 miles from the District of Columbia.

SEC. 772. ACTIVITIES OF THE FOOD AND DRUG ADMINISTRATION.

(a) IN GENERAL.—The Commissioner shall receive and assess the report submitted to the Commissioner by the Executive Director of the Foundation under section 770(l)(2).

(b) REPORT TO CONGRESS.—Beginning with fiscal year 2009, the Commissioner shall submit to Congress an annual report summarizing the incorporation of the information provided by the Foundation in the report described under section 770(l)(2) and by other recipients of grants, contracts, memoranda of understanding, or cooperative agreements into regulatory and product review activities of the Food and Drug Administration.

(c) EXTRAMURAL GRANTS.—The provisions of this subchapter shall have no effect on any grant, contract, memorandum of understanding, or cooperative agreement between the Food and Drug Administration and any other entity entered into before, on, or after the date of enactment of this subchapter.

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CHAPTER IX—MISCELLANEOUS

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SEC. 910. OFFICE OF THE CHIEF SCIENTIST.

(a) ESTABLISHMENT; APPOINTMENT.—The Secretary shall establish within the Office of the Commissioner an office to be known as the Office of the Chief Scientist. The Secretary shall appoint a Chief Scientist to lead such Office.

(b) DUTIES OF THE OFFICE.—The Office of the Chief Scientist shall—

(1) oversee, coordinate, and ensure quality and regulatory focus of the intramural research programs of the Food and Drug Administration;

(2) track and, to the extent necessary, coordinate intramural research awards made by each center of the Administration or science-based office within the Office of the Commissioner, and ensure that there is no duplication of research efforts supported by the Reagan-Udall Foundation for the Food and Drug Administration;

(3) develop and advocate for a budget to support intramural research;

(4) develop a peer review process by which intramural research can be evaluated; and

(5) identify and solicit intramural research proposals from across the Food and Drug Administration through an advisory board composed of employees of the Administration that shall include—

(A) representatives of each of the centers and the science-based offices within the Office of the Commissioner; and

(B) experts on trial design, epidemiology, demographics, pharmacovigilance, basic science, and public health.

BEST PHARMACEUTICALS FOR CHILDREN ACT

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SEC. 6. OFFICE OF PEDIATRIC THERAPEUTICS.

(a) * * *

(b) DUTIES.—The Office of Pediatric Therapeutics shall be responsible for coordination and facilitation of all activities of the Food and Drug Administration that may have any effect on a pedi-

atric population or the practice of pediatrics or may in any other way involve pediatric issues*, including increasing pediatric access to medical devices*.

* * * * * * *

SEC. 14. PEDIATRIC PHARMACOLOGY ADVISORY COMMITTEE.

(a) IN GENERAL.—The Secretary of Health and Human Services shall, under section 222 of the Public Health Service Act (42 U.S.C. 217a) or other appropriate authority, convene and consult an advisory committee on pediatric therapeutics *(including drugs and biological products) and medical devices* (referred to in this section as the "advisory committee").

(b) PURPOSE.—

(1) IN GENERAL.—The advisory committee shall advise and make recommendations to the Secretary, through the Commissioner of Food and Drugs, on matters relating to pediatric therapeutics *(including drugs and biological products) and medical devices*.

(2) MATTERS INCLUDED.—The matters referred to in paragraph (1) include—

(A) pediatric research conducted under sections 351, 409I, and 499 of the Public Health Service Act and sections 501, 502, 505, 505A, [and 505B] *505B, 510(k), 515, and 520(m)* of the Federal Food, Drug, and Cosmetic Act;

[(B) identification of research priorities related to pediatric therapeutics and the need for additional treatments of specific pediatric diseases or conditions; and]

(B) identification of research priorities related to therapeutics (including drugs and biological products) and medical devices for pediatric populations and the need for additional diagnostics and treatments for specific pediatric diseases or conditions;

(C) the ethics, design, and analysis of clinical trials related to pediatric therapeutics *(including drugs and biological products) and medical devices*.

* * * * * * *

(d) CONTINUATION OF OPERATION OF COMMITTEE.—Notwithstanding section 14 of the Federal Advisory Committee Act, the advisory committee shall continue to operate during the five-year period beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007.

SEC. 15. PEDIATRIC SUBCOMMITTEE OF THE ONCOLOGIC DRUGS ADVISORY COMMITTEE.

(a) CLARIFICATION OF AUTHORITIES.—

(1) IN GENERAL.—The Pediatric Subcommittee of the Oncologic Drugs Advisory Committee (referred to in this section as the "Subcommittee"), in carrying out the mission of reviewing and evaluating the data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of pediatric cancers, shall—

(A) * * *

(B) provide recommendations and guidance to help ensure that children with cancer have timely access to the most promising new cancer therapies; [and]

(C) advise on ways to improve consistency in the availability of new therapeutic agents[.]*; and*

(D) provide recommendations to the internal review committee created under section 505A(f) of the Federal Food, Drug, and Cosmetic Act regarding the implementation of amendments to sections 505A and 505B of the Federal Food, Drug, and Cosmetic Act with respect to the treatment of pediatric cancers.

* * * * * * *

(3) CONTINUATION OF OPERATION OF SUBCOMMITTEE.—Notwithstanding section 14 of the Federal Advisory Committee Act, the Subcommittee shall continue to operate during the five-year period beginning on the date of the enactment of the Best Pharmaceuticals for Children Act of 2007.

* * * * * * *

(d) REPORT.—Not later than January 31, [2003] *2009*, the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs and in consultation with the Director of the National Institutes of Health, shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on patient access to new therapeutic agents for pediatric cancer, including access to single patient use of new therapeutic agents.

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PUBLIC HEALTH SERVICE ACT

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TITLE III—GENERAL POWERS AND DUTIES OF PUBLIC HEALTH SERVICE

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PART F—LICENSING—BIOLOGICAL PRODUCTS AND CLINICAL LABORATORIES

Subpart 1—Biological Products

REGULATION OF BIOLOGICAL PRODUCTS

SEC. 351. (a)(1) * * *
(2)(A) * * *

* * * * * * *

(D) RISK EVALUATION AND MITIGATION STRATEGY.—A person that submits an application for a license under this paragraph is subject to section 505(p) of the Federal Food, Drug, and Cosmetic Act.

* * * * * * *

(j) The Federal Food, Drug, and Cosmetic Act, *including the requirements under section 505(p) of such Act,* applies to a biological product subject to regulation under this section, except that a product for which a license has been approved under subsection (a)

shall not be required to have an approved application under section 505 of such Act.

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TITLE IV—NATIONAL RESEARCH INSTITUTES

PART A—NATIONAL INSTITUTES OF HEALTH

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APPOINTMENT AND AUTHORITY OF DIRECTOR OF NIH

SEC. 402. (a) * * *

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[(i)(1)(A) The Secretary, acting through the Director of NIH, shall establish, maintain, and operate a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions (in this subsection referred to as the "data bank"). The activities of the data bank shall be integrated and coordinated with related activities of other agencies of the Department of Health and Human Services, and to the extent practicable, coordinated with other data banks containing similar information.

[(B) The Secretary shall establish the data bank after consultation with the Commissioner of Food and Drugs, the directors of the appropriate agencies of the National Institutes of Health (including the National Library of Medicine), and the Director of the Centers for Disease Control and Prevention.

[(2) In carrying out paragraph (1), the Secretary shall collect, catalog, store, and disseminate the information described in such paragraph. The Secretary shall disseminate such information through information systems, which shall include toll-free telephone communications, available to individuals with serious or life-threatening diseases and conditions, to other members of the public, to health care providers, and to researchers.

[(3) The data bank shall include the following:

[(A) A registry of clinical trials (whether federally or privately funded) of experimental treatments for serious or life-threatening diseases and conditions under regulations promulgated pursuant to section 505(i) of the Federal Food, Drug, and Cosmetic Act, which provides a description of the purpose of each experimental drug, either with the consent of the protocol sponsor, or when a trial to test effectiveness begins. Information provided shall consist of eligibility criteria for participation in the clinical trials, a description of the location of trial sites, and a point of contact for those wanting to enroll in the trial, and shall be in a form that can be readily understood by members of the public. Such information shall be forwarded to the data bank by the sponsor of the trial not later than 21 days after the approval of the protocol.

[(B) Information pertaining to experimental treatments for serious or life-threatening diseases and conditions that may be available—

[(i) under a treatment investigational new drug application that has been submitted to the Secretary under section 561(c) of the Federal Food, Drug, and Cosmetic Act; or

[(ii) as a Group C cancer drug (as defined by the National Cancer Institute).

The data bank may also include information pertaining to the results of clinical trials of such treatments, with the consent of the sponsor, including information concerning potential toxicities or adverse effects associated with the use or administration of such experimental treatments.

[(4) The data bank shall not include information relating to an investigation if the sponsor has provided a detailed certification to the Secretary that disclosure of such information would substantially interfere with the timely enrollment of subjects in the investigation, unless the Secretary, after the receipt of the certification, provides the sponsor with a detailed written determination that such disclosure would not substantially interfere with such enrollment.

[(5) Fees collected under section 736 of the Federal Food, Drug, and Cosmetic Act shall not be used in carrying out this subsection.]

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PART B—GENERAL PROVISIONS RESPECTING NATIONAL RESEARCH INSTITUTES

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[SEC. 409I. PROGRAM FOR PEDIATRIC STUDIES OF DRUGS.

[(a) LIST OF DRUGS FOR WHICH PEDIATRIC STUDIES ARE NEEDED.—

[(1) IN GENERAL.—Not later than one year after the date of enactment of this section, the Secretary, acting through the Director of the National Institutes of Health and in consultation with the Commissioner of Food and Drugs and experts in pediatric research, shall develop, prioritize, and publish an annual list of approved drugs for which—

[(A)(i) there is an approved application under section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j));

[(ii) there is a submitted application that could be approved under the criteria of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j));

[(iii) there is no patent protection or market exclusivity protection under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.); or

[(iv) there is a referral for inclusion on the list under section 505A(d)(4)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(d)(4)(C)); and

[(B) in the case of a drug referred to in clause (i), (ii), or (iii) of subparagraph (A), additional studies are needed to assess the safety and effectiveness of the use of the drug in the pediatric population.

[(2) CONSIDERATION OF AVAILABLE INFORMATION.—In developing and prioritizing the list under paragraph (1), the Secretary shall consider, for each drug on the list—

[(A) the availability of information concerning the safe and effective use of the drug in the pediatric population;

[(B) whether additional information is needed;

[(C) whether new pediatric studies concerning the drug may produce health benefits in the pediatric population; and

[(D) whether reformulation of the drug is necessary.

[(b) CONTRACTS FOR PEDIATRIC STUDIES.—The Secretary shall award contracts to entities that have the expertise to conduct pediatric clinical trials (including qualified universities, hospitals, laboratories, contract research organizations, federally funded programs such as pediatric pharmacology research units, other public or private institutions, or individuals) to enable the entities to conduct pediatric studies concerning one or more drugs identified in the list described in subsection (a).

[(c) PROCESS FOR CONTRACTS AND LABELING CHANGES.—

[(1) WRITTEN REQUEST TO HOLDERS OF APPROVED APPLICATIONS FOR DRUGS LACKING EXCLUSIVITY.—The Commissioner of Food and Drugs, in consultation with the Director of the National Institutes of Health, may issue a written request (which shall include a timeframe for negotiations for an agreement) for pediatric studies concerning a drug identified in the list described in subsection (a)(1)(A) (except clause (iv)) to all holders of an approved application for the drug under section 505 of the Federal Food, Drug, and Cosmetic Act. Such a written request shall be made in a manner equivalent to the manner in which a written request is made under subsection (a) or (b) of section 505A of the Federal Food, Drug, and Cosmetic Act, including with respect to information provided on the pediatric studies to be conducted pursuant to the request.

[(2) REQUESTS FOR CONTRACT PROPOSALS.—If the Commissioner of Food and Drugs does not receive a response to a written request issued under paragraph (1) within 30 days of the date on which a request was issued, or if a referral described in subsection (a)(1)(A)(iv) is made, the Secretary, acting through the Director of the National Institutes of Health and in consultation with the Commissioner of Food and Drugs, shall publish a request for contract proposals to conduct the pediatric studies described in the written request.

[(3) DISQUALIFICATION.—A holder that receives a first right of refusal shall not be entitled to respond to a request for contract proposals under paragraph (2).

[(4) GUIDANCE.—Not later than 270 days after the date of enactment of this section, the Commissioner of Food and Drugs shall promulgate guidance to establish the process for the submission of responses to written requests under paragraph (1).

[(5) CONTRACTS.—A contract under this section may be awarded only if a proposal for the contract is submitted to the Secretary in such form and manner, and containing such agreements, assurances, and information as the Secretary determines to be necessary to carry out this section.

[(6) REPORTING OF STUDIES.—

[(A) IN GENERAL.—On completion of a pediatric study in accordance with a contract awarded under this section, a report concerning the study shall be submitted to the Director of the National Institutes of Health and the Commissioner of Food and Drugs. The report shall include all data generated in connection with the study.

[(B) AVAILABILITY OF REPORTS.—Each report submitted under subparagraph (A) shall be considered to be in the public domain (subject to section 505A(d)(4)(D) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(d)(4)(D)) and shall be assigned a docket number by the Commissioner of Food and Drugs. An interested person may submit written comments concerning such pediatric studies to the Commissioner of Food and Drugs, and the written comments shall become part of the docket file with respect to each of the drugs.

[(C) ACTION BY COMMISSIONER.—The Commissioner of Food and Drugs shall take appropriate action in response to the reports submitted under subparagraph (A) in accordance with paragraph (7).

[(7) REQUESTS FOR LABELING CHANGE.—During the 180-day period after the date on which a report is submitted under paragraph (6)(A), the Commissioner of Food and Drugs shall—

[(A) review the report and such other data as are available concerning the safe and effective use in the pediatric population of the drug studied;

[(B) negotiate with the holders of approved applications for the drug studied for any labeling changes that the Commissioner of Food and Drugs determines to be appropriate and requests the holders to make; and

[(C)(i) place in the public docket file a copy of the report and of any requested labeling changes; and

[(ii) publish in the Federal Register a summary of the report and a copy of any requested labeling changes.

[(8) DISPUTE RESOLUTION.—

[(A) REFERRAL TO PEDIATRIC ADVISORY COMMITTEE.—If, not later than the end of the 180-day period specified in paragraph (7), the holder of an approved application for the drug involved does not agree to any labeling change requested by the Commissioner of Food and Drugs under that paragraph, the Commissioner of Food and Drugs shall refer the request to the Pediatric Advisory Committee.

[(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A), the Pediatric Advisory Committee shall—

[(i) review the available information on the safe and effective use of the drug in the pediatric population, including study reports submitted under this section; and

[(ii) make a recommendation to the Commissioner of Food and Drugs as to appropriate labeling changes, if any.

[(9) FDA DETERMINATION.—Not later than 30 days after receiving a recommendation from the Pediatric Advisory Committee under paragraph (8)(B)(ii) with respect to a drug, the Commissioner of Food and Drugs shall consider the recommendation and, if appropriate, make a request to the holders of approved applications for the drug to make any labeling change that the Commissioner of Food and Drugs determines to be appropriate.

[(10) FAILURE TO AGREE.—If a holder of an approved application for a drug, within 30 days after receiving a request to make a labeling change under paragraph (9), does not agree to make a requested labeling change, the Commissioner may deem the drug to be misbranded under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).

[(11) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under the Federal Food, Drug, and Cosmetic Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

[(12) RECOMMENDATION FOR FORMULATION CHANGES.—If a pediatric study completed under public contract indicates that a formulation change is necessary and the Secretary agrees, the Secretary shall send a nonbinding letter of recommendation regarding that change to each holder of an approved application.]

SEC. 409I. PROGRAM FOR PEDIATRIC STUDIES OF DRUGS.

(a) LIST OF PRIORITY ISSUES IN PEDIATRIC THERAPEUTICS.—

(1) IN GENERAL.—Not later than one year after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary, acting through the Director of the National Institutes of Health and in consultation with the Commissioner of Food and Drugs and experts in pediatric research, shall develop and publish a priority list of needs in pediatric therapeutics, including drugs or indications that require study. The list shall be revised every three years.

(2) CONSIDERATION OF AVAILABLE INFORMATION.—In developing and prioritizing the list under paragraph (1), the Secretary shall consider—

(A) therapeutic gaps in pediatrics that may include developmental pharmacology, pharmacogenetic determinants of drug response, metabolism of drugs and biologics in children, and pediatric clinical trials;

(B) particular pediatric diseases, disorders or conditions where more complete knowledge and testing of therapeutics, including drugs and biologics, may be beneficial in pediatric populations; and

(C) the adequacy of necessary infrastructure to conduct pediatric pharmacological research, including research networks and trained pediatric investigators.

(b) PEDIATRIC STUDIES AND RESEARCH.—The Secretary, acting through the National Institutes of Health, shall award funds to entities that have the expertise to conduct pediatric clinical trials or other research (including qualified universities, hospitals, laboratories, contract research organizations, practice groups, federally funded programs such as pediatric pharmacology research units, other public or private institutions, or individuals) to enable the entities to conduct the drug studies or other research on the issues described in subsection (a). The Secretary may use contracts, grants, or other appropriate funding mechanisms to award funds under this subsection.

(c) PROCESS FOR PROPOSED PEDIATRIC STUDY REQUESTS AND LABELING CHANGES.—

(1) SUBMISSION OF PROPOSED PEDIATRIC STUDY REQUEST.—The Director of the National Institutes of Health shall, as appropriate, submit proposed pediatric study requests for consideration by the Commissioner of Food and Drugs for pediatric studies of a specific pediatric indication identified under subsection (a). Such a proposed pediatric study request shall be made in a manner equivalent to a written request made under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act, including with respect to the information provided on the pediatric studies to be conducted pursuant to the request. The Director of the National Institutes of Health may submit a proposed pediatric study request for a drug for which—

(A)(i) there is an approved application under section 505(j) of the Federal Food, Drug, and Cosmetic Act; or

(ii) there is a submitted application that could be approved under the criteria of such section; and

(B) there is no patent protection or market exclusivity protection for at least one form of the drug under the Federal Food, Drug, and Cosmetic Act; and

(C) additional studies are needed to assess the safety and effectiveness of the use of the drug in the pediatric population.

(2) WRITTEN REQUEST TO HOLDERS OF APPROVED APPLICATIONS FOR DRUGS LACKING EXCLUSIVITY.—The Commissioner of Food and Drugs, in consultation with the Director of the National Institutes of Health, may issue a written request based on the proposed pediatric study request for the indication or indications submitted pursuant to paragraph (1) (which shall include a timeframe for negotiations for an agreement) for pediatric studies concerning a drug identified under subsection (a) to all holders of an approved application for the drug under section 505 of the Federal Food, Drug, and Cosmetic Act. Such a written request shall be made in a manner equivalent to the manner in which a written request is made under subsection (b) or (c) of section 505A of such Act, including with respect to information provided on the pediatric studies to be conducted pursuant to the request and using appropriate formulations for each age group for which the study is requested.

(3) REQUESTS FOR PROPOSALS.—If the Commissioner of Food and Drugs does not receive a response to a written request issued under paragraph (2) not later than 30 days after the date on which a request was issued, the Secretary, acting through the Director of the National Institutes of Health and in consultation with the Commissioner of Food and Drugs, shall publish a request for proposals to conduct the pediatric studies described in the written request in accordance with subsection (b).

(4) DISQUALIFICATION.—A holder that receives a first right of refusal shall not be entitled to respond to a request for proposals under paragraph (3).

(5) CONTRACTS, GRANTS, OR OTHER FUNDING MECHANISMS.—A contract, grant, or other funding may be awarded under this

section only if a proposal is submitted to the Secretary in such form and manner, and containing such agreements, assurances, and information as the Secretary determines to be necessary to carry out this section.

(6) REPORTING OF STUDIES.—

(A) IN GENERAL.—On completion of a pediatric study in accordance with an award under this section, a report concerning the study shall be submitted to the Director of the National Institutes of Health and the Commissioner of Food and Drugs. The report shall include all data generated in connection with the study, including a written request if issued.

(B) AVAILABILITY OF REPORTS.—Each report submitted under subparagraph (A) shall be considered to be in the public domain (subject to section 505A(d)(4) of the Federal Food, Drug, and Cosmetic Act) and shall be assigned a docket number by the Commissioner of Food and Drugs. An interested person may submit written comments concerning such pediatric studies to the Commissioner of Food and Drugs, and the written comments shall become part of the docket file with respect to each of the drugs.

(C) ACTION BY COMMISSIONER.—The Commissioner of Food and Drugs shall take appropriate action in response to the reports submitted under subparagraph (A) in accordance with paragraph (7).

(7) REQUESTS FOR LABELING CHANGE.—During the 180-day period after the date on which a report is submitted under paragraph (6)(A), the Commissioner of Food and Drugs shall—

(A) review the report and such other data as are available concerning the safe and effective use in the pediatric population of the drug studied;

(B) negotiate with the holders of approved applications for the drug studied for any labeling changes that the Commissioner of Food and Drugs determines to be appropriate and requests the holders to make; and

(C)(i) place in the public docket file a copy of the report and of any requested labeling changes; and

(ii) publish in the Federal Register and through a posting on the website of the Food and Drug Administration a summary of the report and a copy of any requested labeling changes.

(8) DISPUTE RESOLUTION.—

(A) REFERRAL TO PEDIATRIC ADVISORY COMMITTEE.—If, not later than the end of the 180-day period specified in paragraph (7), the holder of an approved application for the drug involved does not agree to any labeling change requested by the Commissioner of Food and Drugs under that paragraph, the Commissioner of Food and Drugs shall refer the request to the Pediatric Advisory Committee.

(B) ACTION BY THE PEDIATRIC ADVISORY COMMITTEE.—Not later than 90 days after receiving a referral under subparagraph (A), the Pediatric Advisory Committee shall—

(i) review the available information on the safe and effective use of the drug in the pediatric population, including study reports submitted under this section; and

(ii) make a recommendation to the Commissioner of Food and Drugs as to appropriate labeling changes, if any.

(9) FDA DETERMINATION.—Not later than 30 days after receiving a recommendation from the Pediatric Advisory Committee under paragraph (8)(B)(ii) with respect to a drug, the Commissioner of Food and Drugs shall consider the recommendation and, if appropriate, make a request to the holders of approved applications for the drug to make any labeling change that the Commissioner of Food and Drugs determines to be appropriate.

(10) FAILURE TO AGREE.—If a holder of an approved application for a drug, within 30 days after receiving a request to make a labeling change under paragraph (9), does not agree to make a requested labeling change, the Commissioner of Food and Drugs may deem the drug to be misbranded under the Federal Food, Drug, and Cosmetic Act.

(11) NO EFFECT ON AUTHORITY.—Nothing in this subsection limits the authority of the United States to bring an enforcement action under the Federal Food, Drug, and Cosmetic Act when a drug lacks appropriate pediatric labeling. Neither course of action (the Pediatric Advisory Committee process or an enforcement action referred to in the preceding sentence) shall preclude, delay, or serve as the basis to stay the other course of action.

(d) DISSEMINATION OF PEDIATRIC INFORMATION.—Not later than one year after the date of the enactment of the Best Pharmaceuticals for Children Act of 2007, the Secretary, acting through the Director of the National Institutes of Health, shall study the feasibility of establishing a compilation of information on pediatric drug use and report the findings to Congress.

(e) AUTHORIZATION OF APPROPRIATIONS.—

(1) IN GENERAL.—There are authorized to be appropriated to carry out this section—

(A) $200,000,000 for fiscal year 2008; and

(B) such sums as are necessary for each of the four succeeding fiscal years.

(2) AVAILABILITY.—Any amount appropriated under paragraph (1) shall remain available to carry out this section until expended.

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PART H—GENERAL PROVISIONS

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SEC. 492C. CLINICAL TRIAL REGISTRY DATABASE; CLINICAL TRIAL RESULTS DATABASE.

(a) DEFINITIONS.—In this section:

(1) APPLICABLE CLINICAL TRIAL.—The term "applicable clinical trial"—

(A) means a clinical trial that is conducted to test the safety or effectiveness (including comparative effectiveness) of a drug or device (irrespective of whether the clinical trial is federally or privately funded, and whether the clinical trial involves an approved or unapproved drug or device);

(B) includes such a clinical trial that is conducted outside of the United States if—

(i) there is an application or premarket notification pending before the Food and Drug Administration for approval or clearance of the drug or device involved under section 505, 510(k), or 515 of the Federal Food, Drug, and Cosmetic Act or section 351 of this Act; or

(ii) the drug or device involved is so approved or cleared; and

(C) notwithstanding subparagraphs (A) and (B), excludes—

(i) a clinical trial to determine the safety of a use of a drug that is designed solely to detect major toxicities in the drug or to investigate pharmacokinetics, unless the clinical trial is designed to investigate pharmacokinetics in a special population or populations; and

(ii) a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary focus is feasibility.

(2) CLINICAL TRIAL INFORMATION.—The term "clinical trial information" means those data elements that are necessary to complete an entry in the clinical trial registry database under subsection (b) or the clinical trial results database under subsection (c), as applicable.

(3) COMPLETION DATE.—The term "completion date" means the date of the final collection of data from subjects in the clinical trial for the primary and secondary outcomes to be examined in the trial.

(4) DEVICE.—The term "device" has the meaning given to that term in section 201(h) of the Federal Food, Drug, and Cosmetic Act.

(5) DRUG.—The term "drug" means a drug as defined in section 201(g) of the Federal Food, Drug, and Cosmetic Act or a biological product as defined in section 351 of this Act.

(6) RESPONSIBLE PARTY.—The term "responsible party", with respect to an applicable clinical trial, means—

(A) the primary sponsor (as defined in the International Clinical Trials Registry Platform trial registration data set of the World Health Organization) of the clinical trial; or

(B) the principal investigator of such clinical trial if so designated by such sponsor, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data, has the right to publish the results of the trial, and has the responsibility to meet all of the requirements under this section that are applicable to responsible parties.

(b) CLINICAL TRIALS REGISTRY DATABASE.—

(1) ESTABLISHMENT.—To enhance patient enrollment and provide a mechanism to track subsequent progress of clinical trials, the Secretary, acting through the Director of NIH, shall establish and administer a clinical trial registry database in accordance with this section (referred to in this section as the "registry database"). The Director of NIH shall ensure that the registry database is made publicly available through the Internet.

(2) CONTENT.—The Secretary shall promulgate regulations for the submission to the registry database of clinical trial information that—

(A) conforms to the International Clinical Trials Registry Platform trial registration data set of the World Health Organization;

(B) includes the city, State, and zip code for each clinical trial location or a toll free number through which such location information may be accessed;

(C) includes a statement of the estimated completion date for the clinical trial;

(D) includes the identity and contact information of the responsible party;

(E) if the drug is not approved under section 505 of the Federal Food, Drug, and Cosmetic Act or licensed under section 351 of this Act, or the device is not cleared under section 510(k) or approved under section 515 of the Federal Food, Drug, and Cosmetic Act, specifies whether or not there is expanded access to the drug or device under section 561 of the Federal Food, Drug, and Cosmetic Act for those who do not qualify for enrollment in the clinical trial and how to obtain information about such access;

(F) includes, with respect to any individual who is not an employee of the responsible party for the clinical trial or of the manufacturer of the drug or device involved, information on whether the responsible party or manufacturer has entered into any agreement with such individual that restricts in any manner the ability of the individual—

(i) to discuss the results of the trial at a scientific meeting or any other public or private forum; or

(ii) to publish the results of the trial, or a description or discussion of the results of the trial, in a scientific or academic journal; and

(G) requires the inclusion of such other data elements to the registry database as appropriate.

(3) FORMAT AND STRUCTURE.—

(A) SEARCHABLE CATEGORIES.—The Director of NIH shall ensure that the public may search the entries in the registry database by 1 or more of the following criteria:

(i) The indication being studied in the clinical trial, using Medical Subject Headers (MeSH) descriptors.

(ii) The safety issue being studied in the clinical trial.

(iii) The enrollment status of the clinical trial.

(iv) The sponsor of the clinical trial.

(B) FORMAT.—The Director of the NIH shall ensure that the registry database is easily used by patients, and that entries are easily compared.

(4) DATA SUBMISSION.—The responsible party for an applicable clinical trial shall submit to the Director of NIH for inclusion in the registry database the clinical trial information described in paragraph (2).

(5) TRUTHFUL CLINICAL TRIAL INFORMATION.—

(A) IN GENERAL.—The clinical trial information submitted by a responsible party under this subsection shall not be false or misleading.

(B) EFFECT.—Subparagraph (A) shall not have the effect of requiring clinical trial information to include information from any source other than the clinical trial involved.

(6) TIMING OF SUBMISSION.—Except as provided in paragraph (7), the clinical trial information for a clinical trial required to be submitted under this subsection shall be submitted not later than 14 days after the first patient is enrolled in such clinical trial.

(7) UPDATES.—The responsible party for an applicable clinical trial shall submit to the Director of NIH for inclusion in the registry database periodic updates to reflect changes to the clinical trial information submitted under this subsection. Such updates—

(A) shall be provided not less than once every 6 months until information on the results of the trial is submitted under subsection (c);

(B) shall include identification of the dates of any such changes;

(C) not later than 30 days after the enrollment status of such clinical trial changes, shall include an update of the enrollment status; and

(D) not later than 30 days after the completion date of the clinical trial, shall include a report to the Director that such clinical trial is complete.

(8) APPLICABILITY OF DEVICE TRIALS.—In the case of an applicable clinical trial regarding a device, the responsible person for the trial shall submit to the Director of NIH the clinical trial information as required in paragraph (4), but the Director may not make the information publicly available through the registry database until the device is approved or cleared (as the case may be).

(c) CLINICAL TRIALS RESULTS DATABASE.—

(1) ESTABLISHMENT.—To ensure that results of clinical trials are made public and that patients and providers have current information regarding the results of clinical trials, the Secretary, acting through the Director of NIH, shall establish and administer a clinical trial results database in accordance with this section (referred to in this section as the "results database"). The Director of NIH shall ensure that the results database is made publicly available through the Internet.

(2) SEARCHABLE CATEGORIES.—The Director of NIH shall ensure that the public may search the entries in the results database by 1 or more of the following:

(A) The indication studied in the clinical trial, using Medical Subject Headers (MeSH) descriptors.

(B) The safety issue studied in the clinical trial.

(C) Whether an application for the tested indication is approved, pending approval, withdrawn, or not submitted.

(D) The phase of the clinical trial.

(E) The name of the drug or device that is the subject of the clinical trial.

(F) Within the documents described in clauses (i) and (ii) of paragraph (3)(B), the following information, as applicable:

(i) The sponsor of the clinical trial.

(ii) Each financial sponsor of the clinical trial.

(3) CONTENTS.—

(A) IN GENERAL.—The responsible party for an applicable clinical trial shall submit to the Director of NIH for inclusion in the results database the clinical trial information described in subparagraph (B).

(B) REQUIRED ELEMENTS.—In submitting clinical trial information for a clinical trial to the Director of NIH for inclusion in the results database, the responsible party shall include, with respect to such clinical trial, the following information:

(i) The information described in subparagraphs (A) through (E) of subsection (b)(2).

(ii) A summary that is written in non-technical, understandable language for patients that includes the following:

(I) The purpose of the clinical trial.

(II) The sponsor of the clinical trial.

(III) A point of contact for information about the clinical trial.

(IV) A description of the patient population tested in the clinical trial.

(V) A general description of the clinical trial and results, including a description of and the reasons for any changes in the clinical trial design that occurred since the date of submission of clinical trial information for inclusion in the registry database established under subsection (b) and a description of any significant safety information.

(iii) A summary that is technical in nature that includes the following:

(I) The purpose of the clinical trial.

(II) The sponsor of the clinical trial.

(III) Each financial sponsor of the clinical trial.

(IV) A point of contact for scientific information about the clinical trial.

(V) A description of the patient population tested in the clinical trial.

(VI) A general description of the clinical trial and results, including a description of and the reasons for any changes in the clinical trial design that occurred since the date of submission of clinical trial information for the clinical trial in the registry database established under subsection (b).

(VII) Summary data describing the results, including—

(aa) whether the primary endpoint was achieved, including relevant statistics;

(bb) an assessment of any secondary endpoints, if applicable, including relevant statistics; and

(cc) any significant safety information, including a summary of the incidence of serious adverse events observed in the clinical trial and a summary of the most common adverse events observed in the clinical trial and the frequencies of such events.

(iv) With respect to the group of subjects receiving the drug or device involved, and each comparison group of subjects, the percentage of individuals who ceased participation as subjects and the reasons for ceasing participation.

(v) With respect to an individual who is not an employee of the responsible party for the clinical trial or of the manufacturer of the drug or device involved, information (to the extent not submitted under subsection (b)(2)(F)) on any agreement that the responsible party or manufacturer has entered into with such individual that restricts in any manner the ability of the individual—

(I) to discuss the results of the trial at a scientific meeting or any other public or private forum; or

(II) to publish the results of the trial, or a description or discussion of the results of the trial, in a scientific or academic journal.

(vi) The completion date of the clinical trial.

(vii) A link to the Internet web posting of any adverse regulatory actions taken by the Food and Drug Administration, such as a warning letter, that was substantively based on the clinical trial design, outcome, or representation made by the applicant about the design or outcome of the clinical trial.

(C) LINKS IN DATABASE.—The Director of NIH shall ensure that the results database includes the following:

(i) Links to Medline citations to publications reporting results from each applicable drug clinical trial and applicable device clinical trial.

(ii) Links to the entry for the product that is the subject of an applicable drug clinical trial in the National Library of Medicine database of structured product labels, if available.

(iii) Links described in clauses (i) and (ii) for data bank entries for clinical trials submitted to the data bank prior to enactment of this section, as available.

(4) TIMING.—

(A) IN GENERAL.—Except as provided in subparagraphs (B) and (C), a responsible party shall submit to the Director of NIH for inclusion in the results database clinical trial information for an applicable clinical trial not later than 1 year after the earlier of—

(i) the estimated completion date of the trial, as submitted under subsection (b)(2); or

(ii) the actual date of the completion, or termination before completion, of the trial, as applicable.

(B) EXTENSIONS.—The Director of NIH may provide an extension of the deadline for submission of clinical trial information under subparagraph (A) if the responsible party for the trial submits to the Director a written request that demonstrates good cause for the extension and provides an estimate of the date on which the information will be submitted. The Director of NIH may grant more than one such extension for the clinical trial involved.

(C) UPDATES.—The responsible party for an applicable clinical trial shall submit to the Director of NIH for inclusion in the results database periodic updates to reflect changes in the clinical trial information submitted under this subsection. Such updates—

(i) shall be provided not less frequently than once every 6 months during the 10-year period beginning on the date on which information is due under subparagraph (A);

(ii) shall identify the dates on which the changes were made; and

(iii) shall include, not later than 30 days after any change in the regulatory status of the drug or device involved, an update informing the Director of NIH of such change.

(5) TRUTHFUL CLINICAL TRIAL INFORMATION.—

(A) IN GENERAL.—The clinical trial information submitted by a responsible party under this subsection shall not be false or misleading in any particular.

(B) EFFECT.—Subparagraph (A) shall not have the effect of requiring clinical trial information with respect to a clinical trial to include information from any source other than such clinical trial.

(6) PUBLIC AVAILABILITY OF RESULTS.—

(A) PRE-APPROVAL STUDIES.—Except as provided in subparagraph (E), with respect to an applicable clinical trial that is completed before the drug is initially approved under section 505 of the Federal Food, Drug, and Cosmetic Act or initially licensed under section 351 of this Act, or the device is initially cleared under section 510(k) or approved under section 515 of the Federal Food, Drug, and Cosmetic Act, the Director of NIH shall make publicly available on the results database the clinical trial information submitted for such clinical trial not later than 30 days after—

(i) the drug or device is approved under such section 505, licensed under such section 351, cleared under such section 510(k), or approved under such section 515, as applicable; or

(ii) the Secretary issues a not approvable letter or a not substantially equivalent letter for the drug or device under such section 505, 351, 510(k), or 515, as applicable.

(B) MEDICAL AND CLINICAL PHARMACOLOGY REVIEWS OF PRE-APPROVAL STUDIES.—Not later than 90 days after the date applicable under clause (i) or (ii) of subparagraph (A) with respect to an applicable clinical trial, the Director of NIH shall make publicly available on the results database

a summary of the available medical and clinical pharmacology reviews conducted by the Food and Drug Administration for such trial.

(C) POST-APPROVAL STUDIES.—Except as provided in subparagraphs (D) and (E), with respect to an applicable clinical trial that is completed after the drug is initially approved under such section 505 or licensed under such section 351, or the device is initially cleared under such section 510(k) or approved under such section 515, the Director of NIH shall make publicly available on the results database the clinical trial information submitted for such clinical trial not later than 30 days after the date of such submission.

(D) SEEKING APPROVAL OF A NEW USE FOR THE DRUG OR DEVICE.—

(i) IN GENERAL.—If the manufacturer of the drug or device is the sponsor or a financial sponsor of an applicable clinical trial, and such manufacturer certifies to the Director of NIH that such manufacturer has filed, or will file within 1 year, an application seeking approval under such section 505, licensing under such section 351, clearance under such section 510(k), or approval under such section 515 for the use studied in such clinical trial (which use is not included in the labeling of the approved drug or device), then the Director of NIH shall make publicly available on the results database the clinical trial information submitted for such clinical trial on the earlier of the date that is 30 days after the date—

(I) the new use of the drug or device is approved under such section 505, licensed under such section 351, cleared under such section 510(k), or approved under such section 515;

(II) the Secretary issues a not approvable letter or a not substantially equivalent letter for the new use of the drug or device under such section 505, 351, 510(k), or 515; or

(III) the application or premarket notification under such section 505, 351, 510(k), or 515 is withdrawn.

(ii) LIMITATION ON CERTIFICATION.—If a manufacturer makes a certification under clause (i) with respect to a clinical trial, the manufacturer shall make such a certification with respect to each applicable clinical trial that is required to be submitted in an application for approval of the use studied in the clinical trial.

(iii) 2-YEAR LIMITATION.—The clinical trial information subject to clause (i) shall be made publicly available on the results database on the date that is 2 years after the date the certification referred to in clause (i) was made to the Director of NIH, if a regulatory action referred to in subclause (I), (II), or (III) of clause (i) has not occurred by such date.

(iv) MEDICAL AND CLINICAL PHARMACOLOGY REVIEWS.—Not later than 90 days after the date applica-

ble under subclause (I), (II), or (III) of clause (i) or clause (iii) with respect to an applicable clinical trial, the Director of NIH shall make publicly available on the results database a summary of the available medical and clinical pharmacology reviews conducted by the Food and Drug Administration for such trial.

(E) SEEKING PUBLICATION.—

(i) IN GENERAL.—If the principal investigator of an applicable clinical trial is seeking publication in a peer-reviewed biomedical journal of a manuscript based on the results of the clinical trial and the responsible party so certifies to the Director of NIH—

(I) the responsible party shall notify the Director of NIH of the publication date of such manuscript not later than 15 days after such date; and

(II) the Director of NIH shall make publicly available on the results database the clinical trial information submitted for such clinical trial on the date that is 30 days after the publication date of such manuscript.

(ii) LIMITATIONS.—The clinical trial information subject to clause (i)—

(I) shall be made publicly available on the results database on the date that is 2 years after the date that the clinical trial information was required to be submitted to the Director of NIH if the manuscript referred to in such clause has not been published by such date; and

(II) shall not be required to be made publicly available under section 552 of title 5, United States Code (commonly known as the "Freedom of Information Act"), prior to the date applicable to such clinical trial information under this subparagraph.

(7) VERIFICATION OF SUBMISSION PRIOR TO PUBLIC AVAILABILITY.—In the case of clinical trial information that is submitted under this subsection, but is not made publicly available pending either regulatory action or publication under subparagraph (D) or (E) of paragraph (6), as applicable, the Director of NIH shall respond to inquiries from other Federal agencies and peer-reviewed journals to confirm that such clinical trial information has been submitted but has not yet been made publicly available on the results database.

(d) UPDATES; TRACKING OF CHANGES IN SUBMITTED INFORMATION.—The Director of NIH shall ensure that updates submitted to the Director under subsections (b)(7) and (c)(4) do not result in the removal from the registry database or the results database of the original submissions or of any preceding updates, and that information in such databases is presented in a manner that enables users to readily access each original submission and to track the changes made by the updates.

(e) COORDINATION AND COMPLIANCE.—

(1) CONSULTATION WITH OTHER FEDERAL AGENCIES.—The Secretary shall—

(A) consult with other agencies that conduct human studies in accordance with part 46 of title 45, Code of Federal Regulations (or any successor regulations), to determine if any such studies are applicable clinical trials; and

(B) develop with such agencies appropriate procedures to ensure that clinical trial information for such applicable clinical trials is submitted under subsection (b) and (c).

(2) COORDINATION OF REGISTRY DATABASE AND RESULTS DATABASE.—

(A) IN GENERAL.—Each entry in the registry database under subsection (b) or the results database under subsection (c) shall include a link to the corresponding entry in the results database or the registry database, respectively.

(B) MISSING ENTRIES.—

(i) IN GENERAL.—If, based on a review of the entries in the registry database under subsection (b), the Director of NIH determines that a responsible party has failed to submit required clinical trial information to the results database under subsection (c), the Director of NIH shall inform the responsible party involved of such failure and permit the responsible party to correct the failure within 30 days.

(ii) FAILURE TO CORRECT.—If the responsible party does not correct a failure to submit required clinical trial information within the 30-day period described under clause (i), the Director of NIH shall report such noncompliance to the scientific peer review committees of the Federal research agencies and to the Office of Human Research Protections.

(iii) PUBLIC NOTICE OF FAILURE TO CORRECT.—The Director of NIH shall include in the clinical trial registry database entry and the clinical trial results database entry for each applicable clinical trial a notice of any uncorrected failure to submit required clinical trial information and shall provide that the public may easily search for such entries.

(3) ACTION ON APPLICATIONS.—

(A) VERIFICATION PRIOR TO FILING.—The Secretary, acting through the Commissioner of Food and Drugs, shall verify that the clinical trial information required under subsections (b) and (c) for an applicable clinical trial is submitted pursuant to such subsections, as applicable—

(i) when considering a drug or device for an exemption under section 505(i) or section 520(g) of the Federal Food, Drug, and Cosmetic Act; and

(ii) prior to filing an application or premarket notification under section 505, 510(k), or 515 of the Federal Food, Drug, and Cosmetic Act or section 351 of this Act, that includes information from such clinical trial.

(B) NOTIFICATION.—If the Secretary determines under subparagraph (A) that clinical trial information has not been submitted as required by subsection (b) or (c), the Secretary shall notify the applicant and the responsible party

of such noncompliance and require submission of such information within 30 days.

(C) REFUSAL TO FILE.—If the responsible party does not remedy such noncompliance within 30 days of receipt of notification under subparagraph (B), the Secretary shall refuse to file, approve, or clear such application or premarket notification.

(4) CONTENT REVIEW.—

(A) IN GENERAL.—To ensure that the summary documents described in subsection (c)(3) are non-promotional, and are not false or misleading in any particular under subsection (c)(5), the Secretary shall compare such documents to the results data of the clinical trial for a representative sample of applicable clinical trials by—

(i) acting through the Commissioner of Food and Drugs to examine the results data for such clinical trials submitted to Secretary when such data are submitted—

(I) for review as part of an application under section 505 or 515 of the Federal Food, Drug, and Cosmetic Act or under section 351 of this Act or a premarket notification under section 510(k) of the Federal Food, Drug, and Cosmetic Act; or

(II) in an annual status report on the drug or device under such application;

(ii) acting with the Federal agency that funds such clinical trial in whole or in part by a grant to examine the results data for such clinical trials; and

(iii) acting through inspections under section 704 of the Federal Food, Drug, and Cosmetic Act to examine results data for such clinical trials not described in clause (i) or (ii).

(B) NOTICE OF NONCOMPLIANCE.—If the Secretary determines that the clinical trial information submitted in such a summary document is false or misleading in any particular, the Secretary shall notify the responsible party and give such party an opportunity to remedy such noncompliance by submitting the required revised clinical trial information within 30 days of such notification.

(f) PENALTIES FOR NONCOMPLIANCE.—

(1) IN GENERAL.—The following acts and the causing thereof are unlawful:

(A) The failure to submit clinical trial information as required by this section.

(B) The submission of clinical trial information under this section that is false or misleading in any particular in violation of subsection (b)(5) or (c)(5).

(2) CERTAIN PENALTIESSection 303(a) of the Federal Food, Drug, and Cosmetic Act applies with respect to a violation of paragraph (1) to the same extent and in the same manner as such section 303(a) applies with respect to a violation of section 301 of such Act.

(3) CONSIDERATIONS.—In determining whether to apply a penalty under paragraph (2) or under paragraph (4) for a viola-

tion described in paragraph (1), the Secretary, acting through the Commissioner of Food and Drugs, shall consider—

(A) whether the responsible party promptly corrects the noncompliance when provided notice;

(B) whether the responsible party has engaged in a pattern or practice of noncompliance; and

(C) the extent to which the noncompliance involved may have significantly misled health care providers or patients concerning the safety or effectiveness of the drug involved.

(4) CIVIL PENALTIES.—

(A) IN GENERAL.—A person is subject to a civil penalty in accordance with this paragraph if the person commits a violation described in paragraph (1) and fails to correct the violation by the end of the 30-day period described in subparagraph (B).

(B) NOTIFICATION.—If a person is in violation of paragraph (1), the Secretary shall notify the person of such noncompliance and give the person a 30-day period to correct such violation before imposing a civil penalty under this paragraph.

(C) AMOUNT OF PENALTY.—The amount of a civil penalty under this subsection shall be not more than a total of $15,000 for all violations adjudicated in a single proceeding in the case of an individual, and not more than $10,000 per day until the violation is corrected in the case of any other person, except that if the person is a nonprofit entity the penalty may not exceed a total of $15,000 for all violations adjudicated in a single proceeding.

(D) PROCEDURES.—The provisions of paragraphs (4) through (6) of section 303(f) of the Federal Food, Drug, and Cosmetic Act apply to the imposition of a penalty under this subsection to the same extent and in the same manner as such provisions apply to a penalty imposed under such section 303(f).

(g) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated to carry out this section $10,000,000 for each fiscal year.

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PART I—FOUNDATION FOR THE NATIONAL INSTITUTES OF HEALTH

SEC. 499. ESTABLISHMENT AND DUTIES OF FOUNDATION.

(a) * * *

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(c) CERTAIN ACTIVITIES OF FOUNDATION.—

(1) IN GENERAL.—In carrying out subsection (b), the Foundation may solicit and accept gifts, grants, and other donations, establish accounts, and invest and expend funds in support of the following activities with respect to the purpose described in such subsection:

(A) * * *

* * * * * * *

(C) A program to collect funds for pediatric pharmacologic research [and studies listed by the Secretary pursuant to section 409I(a)(1)(A) of this Act and referred under section 505A(d)(4)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a(d)(4)(C))].

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ORPHAN DRUG ACT

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GRANTS AND CONTRACTS FOR DEVELOPMENT OF DRUGS FOR RARE DISEASES AND CONDITIONS

SEC. 5. (a) * * *

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[(c) For grants and contracts under subsection (a), there are authorized to be appropriated such sums as already have been appropriated for fiscal year 2002, and $25,000,000 for each of the fiscal years 2003 through 2006.]

(c) For grants and contracts under subsection (a), there is authorized to be appropriated $30,000,000 for each of fiscal years 2008 through 2012.

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ADDITIONAL VIEWS

We support the goal and concept of enhancing access to information on clinical trials and providing a mechanism to enable health care professionals and the public to obtain information about trial results. In Committee Mr. Deal offered and withdrew an amendment which would accomplish our mutual objectives but leaves the Department of Health and Human Services the flexibility they need and requested to go forward.

The current legislation presents significant conceptual and operational problems that need to be resolved if such proposed databases are to prove feasible. The proposed legislation requires the Department not only to monitor, track, and verify data submissions, and determine if and when certain trial information can be released, but to undertake numerous regulatory functions not associated with current NIH and FDA systems, such as notifying responsible parties of non-compliance in data submission, monitoring subsequent performance to assure compliance, and, as necessary, taking certain compliance-related enforcement actions.

The implementation challenges associated with establishing the results database would be daunting, particularly given the ambitious timeframes outlined in the bill.

The proposed results database would contain large volumes of information—including summary reports intended for use by patients and clinicians—that have not been subject to external, scientific review.

It is critical that such a database be defined in a way that recognizes the potential risks of posting unvalidated information and the difficulty of ensuring the accuracy and completeness of submitted data, and that accommodates the operational and resource limitations of NIH, FDA, and other federal agencies.

The approach in the other body is a better starting point. We think it is important to set out a trial period for NIH to get further experience with a results data base. HHS would then provide regulatory authority to set out the requirements for such a data base.

We do share the basic objectives of the authors. We believe there is a commitment from the authors and the Full Committee and Subcommittee Chairman to continue to work to a more workable model.

We believe the bill as written may pose significant problems in a year. People will not know how to comply. There will be too many ambiguities. Methods for summarizing data, where such methods are not validated, will end up misinforming people. We know that is not our intention. At some point, it is useful to recognize the limitations of micromanaging efforts like this.

JOE BARTON.
NATHAN DEAL.

ADDITIONAL VIEWS

We strongly support this legislation to implement an aggressive post-market drug safety regulatory framework at the Food and Drug Administration (FDA) to better ensure the safety of the nation's drug supply. While we believe that Congress should enact these measures to protect the American public from adverse drug events, we are concerned that this legislation fails to adequately ensure consumers' continued access to State remedies in the event of personal injury or wrongful death from a pharmaceutical product regulated under this bill.

Specifically, we are concerned about the unintended consequence of triggering field preemption, whereby a defendant could argue that this legislation creates a pervasive regulatory scheme under which the defendant could gain immunity from State liability claims. The additional regulation of pharmaceutical products proposed in this legislation is an effort to provide consumers with increased protection, not an effort to provide pharmaceutical manufacturers with immunity from liability when their products harm consumers. In no way do we intend to occupy this regulatory field to an extent that would limit the right of consumers to seek civil compensation in the event of personal injury or wrongful death resulting from a finding of liability on the part of pharmaceutical manufacturers.

To address any unintended consequences this legislation may impose upon a consumer's access to State remedies, we support the future inclusion of language to clarify that nothing in this legislation or in current law is intended to preempt remedies for consumers injured by dangerous drugs. With the inclusion of this language, Congress would strike the appropriate balance between providing the FDA with the necessary authority to protect consumers from adverse drug events and ensuring that Congress does not inadvertently preempt common law remedies. Such language would preserve the status quo, allowing the FDA and state remedies to remain complementary and necessary safeguards to protect American families.

We look forward to working with the Chairman and conferees to ensure that consumers are protected from the consequences of dangerous or deadly drugs.

GENE GREEN.
LOIS CAPPS.
JAY INSLEE.
BART STUPAK.
JANICE SCHAKOWSKY.
HENRY A. WAXMAN.
DIANA DEGETTE.
CHARLES A. GONZALEZ.
MIKE DOYLE.

HILDA L. SOLIS.
THOMAS ALLEN.
TAMMY BALDWIN.
JOHN BARROW.
MIKE ROSS.
ANTHONY WEINER.

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