## SECTION-BY-SECTION ANALYSIS OF THE LEGISLATION

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## 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the Secretary of Health and Human Services will retain 25 percent of the application fees for applications that are withdrawn before filing; and that applications or supplements previously refused for filing or that were withdrawn before filing will be subject to the full user fee upon being resubmitted or filed over protest, unless otherwise exempted or waived.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 triggered 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-employee 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 address 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 approved 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 Secretary 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 Commissioners 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 review 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 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 shall 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 various 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 r*esponsible 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 information 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 under-representation 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 participate 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 access 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 available 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.