The Food and Drug Administration Safety and Innovation Act
Manager's Amendment
April 23, 2012

TITLE I—FEES RELATING TO DRUGS

Title I (PDUFA V) would reauthorize the prescription drug user fee program, allowing the Secretary to continue to collect fees from industry to support the review process for human drug applications, as specified in the law, from FY2013 through FY2017. This title would set total PDUFA fee revenue for FY2013 at $693 million, 1.3% below the $702 million in PDUFA fees in the FY2012 budget. It would continue the three types of fees—application, establishment, and product. It would modify the formula for calculating annual inflation adjustments to better reflect personnel and benefits costs to FDA and use fewer preceding years in the calculation's base. User fee authority would sunset on October 1, 2017.

TITLE II—FEES RELATING TO DEVICES

Title II (MDUFA III) would reauthorize the medical device user fee program, allowing a total of $595 million in fees to be collected from industry over the five year period of FY2013 through FY2017. The title would change the definition of "establishment subject to a registration fee," increasing the number of establishments paying the fee. The establishment fee would be $2,575 in FY2013 and rise to $3,872 for FY2016/FY2017. Except for the establishment fee, the amount of each type of user fee (e.g., 510(k) fee) is set as a percentage of the PMA fee, also called the base fee. The base fee would be $248,000 in FY2013 and would rise to $268,443 for FY2017. The 510(k) fee would change from 1.84% to 2% of the base fee; all other fee percentages would be the same as in current law. Fee amounts would be adjusted for inflation. The bill would allow the waiver or reduction of fees for a PMA or establishment fee "if the waiver is in the interest of public health." The fee waiver is intended for laboratory developed test manufacturers. The bill would authorize streamlined hiring of employees; this authority would end three years after enactment of this section. User fee authority would sunset on October 1, 2017.

TITLE III—FEES RELATING TO GENERIC DRUGS

Title III (GDUFA) would authorize a new generic drug user fee program, allowing the Secretary to collect fees from industry to support the human generic drug approval activities, as specified. This title would authorize the Secretary to collect $299 million each year from FY2013 through FY2017 in fees from the generic drug industry and provides formulas for calculating inflation adjustments for the later years. For the first year of the program, $50 million of the $299 million would come from a one-time backlog fee to be paid by sponsors of currently pending applications. Fee types that would apply each year, and their percentage of generic user fee collections, are the drug master file fee (6%); the abbreviated new drug application (ANDA) and prior approval supplement fees (24%); the generic drug facility fee (56%); and the active pharmaceutical ingredient facility fee (14%).

Title III would set limits to ensure that fees supplement rather than replace appropriations. Budget authority (appropriations minus fees) would remain at least at the FY2009 level, adjusted for inflation, for (1) FDA salaries and expenses overall and (2) human generic drug activities (which the bill defines). Other provisions include risk-based biennial inspections, parity of domestic and foreign inspection schedules by FY2017, a $15,000 to $30,000 higher inspection fee for a foreign versus domestic facility to reflect cost differences, streamlined hiring authority, and required annual performance and fiscal reports. The generic drug user fee authority would sunset on October 1, 2017.

TITLE IV—FEES RELATING TO BIOSIMILAR BIOLOGICAL PRODUCTS

Title IV (BSUFA) would authorize a new biosimilars user fee program and would require the collection of six different types of fees from industry. Fee amounts would be based on inflation-adjusted PDUFA fee amounts for each fiscal year. The "initial biosimilar biological product development fee" would be 10% of the human drug application fee under PDUFA. The "annual biosimilar biological product development fee" would be 10% of the human drug application fee. The "reactivation fee" would be 20% of the human drug application fee. The "biosimilar biological product application fee" would equal the human drug application fee minus the cumulative amount paid for product development program fees. The "biosimilar biological product establishment fee" would be equal to the prescription drug establishment fee under PDUFA. The "biosimilar biological product fee" would be equal to the prescription drug product fee under PDUFA. The title would require the Secretary to waive the biosimilar biological product application fee for the first such application from a small business. A "small business" is as an entity with fewer than 500 employees that does not have a drug product that has been approved under a human drug or biosimilar biological application and introduced or delivered for introduction into commerce. The title also requires annual performance and fiscal reports. The biosimilars user fee authority would sunset on October 1, 2017.

TITLE V—PEDIATRIC DRUGS AND DEVICES

Sec. 501 would make permanent the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA).

Sec. 502 would clarify the Secretary's authority to award exclusivity for studies conducted pursuant to a written request, including a conforming change for biological products.

Sec. 503 would require the Secretary to issue guidance providing for Pediatric Review Committee (PeRC) review of any significant modifications made to written requests or pediatric study plans.

Sec. 504 would require the Secretary, within three years of enactment, to make public the medical, statistical, and clinical pharmacology reviews of written requests made between 2002 and 2007 that resulted in a labeling change.

Sec. 505 would allow for extensions of pediatric study deadlines in appropriate circumstances. Current tracking requirements would be expanded to collect data about deferral extensions and the timeline to completion of assessments. If a required pediatric study was not completed or deferred, the Secretary would issue a letter and require a response within 45 days, both of which would be made publicly available.

Sec. 506 would tie the submission of an initial pediatric study plan to the sponsor's end of the phase 2 meeting with FDA, unless the Secretary and the applicant agree to an alternative date. The requirements and process for pediatric study plan submissions would be further clarified through regulations.

Sec. 507 would permanently reauthorize the Pediatric Advisory Committee, reauthorize the Pediatric Subcommittee of the Oncologic Drug Advisory Committee (ODAC) in a manner consistent with the authorization of ODAC, reauthorize the Humanitarian Device Exemption Extension through 2017, reauthorize Demonstration Grants to Improve Pediatric Device Availability through 2017, and permanently reauthorize the Program for Pediatric Study of Drugs.

Sec. 508 would require a report every five years evaluating the effectiveness of BPCA and PREA.

Sec. 509 makes technical changes.

Sec.510 would clarify that labeling changes made as a result of a study that was inconclusive or did not demonstrate that the product is safe or effective do not qualify for three years of statutory exclusivity.

TITLE VI—MEDICAL DEVICE REGULATORY IMPROVEMENTS

Sec. 601 would allow the Secretary, based on new information, to change the classification of a device by administrative order instead of by regulation; authority to issue the order is non-delegable by the FDA Commissioner.

Sec. 602 would codify the Secretary's authority to require, as a condition of premarket approval, postmarket study regarding the device.

Sec. 603 would clarify the Secretary's authority to order postmarket surveillance for specified Class II and III devices either at the time of their approval or clearance, or at any time thereafter. A manufacturer would be required to start an ordered postmarket surveillance no later than 15 months after the order.

Sec. 604 would require the Secretary to extend its "Sentinel" postmarket risk identification and evaluation system to include medical devices, and, when implementing this system, to engage stakeholders.

Sec. 605 would require the Secretary to create a program to assess information submitted or reported pursuant to device recalls, removals and corrections and to use this information to identify strategies for mitigating health risks from defective or unsafe devices. The Secretary would be required to clarify procedures for device recall audit checks and develop criteria for assessing correction or removal actions.

Sec. 606 would allow the Secretary to issue a clinical hold prohibiting the sponsor of a medical device from conducting a clinical investigation using the device if the Secretary determines the device represents an unreasonable risk to the subjects' safety or for other reasons established by regulation. A sponsor requesting a removal of a clinical hold would be required to receive a written decision within 30 days.

Sec. 607 would require the Secretary to issue proposed regulations establishing a unique device identification system by no later than December 31, 2012, finalize the regulation within six months of the close of the comment period, and implement such a system within 2 years for certain devices.

Sec. 608 would clarify the statutory "least burdensome" standard by providing that the requirement in current law that certain clinical data requests be "necessary" means that the request be limited, for PMA applications, to the minimum required to demonstrate the effectiveness of a device for the conditions of use and, for 510(k) notifications, to the minimum required to support a determination of substantial equivalence between a new and a predicate device.

Sec. 609 would clarify the FDA's policy on customization of devices for small (five or fewer per year), unique populations. If a device is not available in the U.S. and no other devices are domestically available to treat the specific patient, it does not have to comply with the premarket approval requirements for devices if it is intended to meet the special needs of a physician and is manufactured on a case-by-case basis to accommodate the unique physiology.

Sec. 610 would require the Secretary to provide a summary of the scientific and regulatory rationale for a decision to deny clearance of a 510(k) notification; approval of a PMA application; or disapproval of an IDE application. Within 30 days of receiving such a denial, the recipient may request a supervisory review of the decision. The Secretary would be required to follow a specified timeframe for review, except in cases involving consultation with outside experts or cases involving evidence not in the record at the time of the denial.

Sec. 611 would clarify that notices that set forth changes in interpretations of a regulation or policy, including notice to industry letters, are guidance documents subject to FDA's good guidance practice rules.

Sec. 612 would allow the Secretary to classify certain new devices without predicates into class I or II without first issuing a determination that they are not substantially equivalent (NSE) if the devices meets certain risk classification criteria. The Secretary could decline this de novo classification request if the device was not low-moderate risk or if there was in existence a legally marketed device on which to base FDA review.

Sec. 613 would expand the exemption from the prohibition on profit for devices that have been granted Humanitarian Device Exemptions to include devices intended for use in adults if the device is intended for the treatment or diagnosis of a disease or condition that does not occur in pediatric patients, or that occurs in such numbers that the device's development is impossible, highly impracticable, or unsafe. The annual distribution number permitted for HDE devices would be altered to the number of devices needed to treat, diagnose or cure 4,000 individuals in the United States during any calendar year.

Sec. 614 would reauthorize, through October 1, 2017, accredited third party review of 510(k) submissions and third-party inspections of factory, warehouse, or manufacturing or processing establishments.

Sec. 615 would require the FDA to withdraw its recent guidance, "Guidance for Industry and FDA Staff - 510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device," due to the agency's acknowledgement of potential unintended consequences that may result from its implementation. The Secretary must ensure that affected stakeholders are provided with an opportunity to comment before any future guidance document on this issue is made final.

TITLE VII—DRUG SUPPLY CHAIN

Sec. 701 would expand the information required of registrants engaged in the manufacture, preparation, propagation, compounding, or processing of drugs, to include each facility's unique facility identifier, point-of-contact e-mail address, and specified information about each drug importer that takes physical possession of a drug, other than an excipient.

Sec. 702 would require registration by foreign facilities that manufacture, prepare, propagate, compound, or process drugs, by deeming drugs from an unregistered facility misbranded. It would amend registration requirements to include a unique facility identifier and point-of-contact e-mail address, and to include similar information about each drug importer and the importer's establishments.

Sec. 703 would expand the required product listing information to also include information on drug excipient establishments, including a unique facility identifier and point-of-contact e-mail address.

Sec. 704 would require that, after specifying a unique facility identifier system, the Secretary maintain an electronic database. It also would require the Secretary to ensure the accuracy and coordination of FDA databases in order to identify and inform risk-based inspections.

Sec. 705 would require the Secretary to carry out drug facility inspections according to a risk-based schedule (with risks specified), and to not distinguish between prescription and nonprescription drug products.

Sec. 706 would require a manufacturer to submit certain records required for inspection, upon the request of the Secretary, in a timely and reasonable manner at the manufacturer's expense; and would require the Secretary to clearly describe records requested and to provide a confirmation receipt.

Sec. 707 would require the Secretary of Homeland Security, upon request from the HHS Secretary, to refuse to admit into the United States a drug product manufactured in an establishment that has refused to permit HHS inspection.

Sec. 708 would protect drug-related information obtained by the Secretary from disclosure under the Freedom of Information Act and other laws, when such information is provided by a federal, state, local, or foreign government agency that has requested that the information be kept confidential. In specified circumstances, the Secretary may share certain drug-related trade secret information through written agreement with foreign governments that the Secretary has certified as able to protect trade secret information from disclosure.

Sec. 709, with respect to criteria for determining a drug to be adulterated, would clarify that "current good manufacturing practices" include quality controls in manufacturing, and assurance of raw material safety.

Sec. 710 would require the Secretary to establish an accreditation system, to include the recognition of accreditation bodies and the development of model standards, for third party auditors to conduct safety and quality audits that may be used to certify compliance with good manufacturing practices, documentation requirements at the border, and other purposes as determined by the Secretary. The Secretary shall use the results of the audits to inform the drug risk-based inspection schedule. The Secretary could directly grant or revoke accreditation of third-party auditors, including foreign governments. Accredited auditors would be required to provide audit findings to FDA upon request, and to report to the Secretary any conditions that pose a serious risk to public health.

Sec. 711 would allow the Secretary to require electronic submission of certain information by a drug importer as a condition of granting entry. Such information could include regulatory status, facility information (including unique facility identifier), and inspection and compliance information. The Secretary must take into consideration the type of import, such as whether the drug is for import into the United States for use in preclinical or clinical investigation.

Sec. 712 would allow the Secretary to require notification by persons required to register as establishments engaged in manufacture, preparation, propagation, compounding, or processing of a drug, as well as persons engaged in wholesale distribution, if such persons know (1) of a substantial loss or theft of the drug, or (2) the drug has been or is being counterfeited and the counterfeit product is either in U.S. commerce or is offered for import into the United States. Notification requirements apply to such losses, thefts, or counterfeiting that occur on or after the date of enactment. The failure to notify the Secretary would be a prohibited act, which could subject the person to penalties.

Sec. 713 would allow the HHS Secretary, in collaboration with the Secretary of Homeland Security, to destroy drugs refused admission that have a reasonable probability of causing serious adverse health consequences or death to humans or animals, as well as drugs valued at $2,000 or less. This amendment would not take effect until the HHS Secretary issues regulations providing the owner or consignee with notice and an opportunity to introduce testimony and appear before the HHS Secretary prior to the destruction of such drugs.

Sec. 714 would enhance the penalty to not more than 20 years imprisonment or a fine of not more than $1 million, or both, for any person who knowingly and intentionally adulterates a drug under certain statutory definitions of adulteration if the drug has a reasonable probability of causing serious adverse health consequences or death to humans or animals.

Sec. 715 would enhance the penalty to not more than 20 years imprisonment or a fine of not more than $4 million, or both, for persons who knowingly and intentionally commit certain prohibited acts related to forging and counterfeiting of drugs, including selling and dispensing.

Sec. 716 would make extraterritorial violations of the FFDCA subject to enforcement in the United States if either (1) the article related to the violation was intended for import into the United States, or (2) an act in furtherance of the violation was committed in the United States.

Sec. 717 would require courts and administrative agencies to interpret and apply Title VII of the bill consistent with international agreements to which the United States is a party.

TITLE VIII—GENERATING ANTIBIOTIC INCENTIVES NOW

This title would address the availability of new drugs to treat infectious diseases through market and regulatory incentives.

Sec. 801 would provide incentives for development of new qualified infectious disease products (QIDPs) by providing an additional five years of market exclusivity, in addition to the periods of exclusivity for which such drugs would otherwise qualify. Sec. 801 defines QIDPs as antibacterial or antifungal drugs intended to treat serious or life-threatening infections, including those caused by qualifying pathogens, which would be listed and revised by the Secretary through regulation. Sec. 801 would require final regulations within two years of enactment.

Sec. 802 would make QIDPs eligible for priority review and Sec. 803 would make them eligible for fast track review.

Sec. 804 would require a GAO study of the need for incentives and possible regulatory issues, including an assessment of regulatory, review, and development QIDP issues.

Sec. 805 would require the Secretary to review and, if needed, to update guidance documents regarding the conduct of clinical trials for antibacterial and antifungal drugs, and would allow the Secretary to provide written recommendations for such trials, upon the request of a sponsor seeking approval of a QIDP. The section would require a GAO study of clinical trial guidance documents.

Sec. 806 would require the Secretary to report to Congress with a strategy and implementation plan regarding the requirements of this title, and to later report on the number and list of QIDPs, as well as QIDP submissions, approvals, and review times.

TITLE IX—DRUG APPROVAL AND PATIENT ACCESS

This title would require the Secretary to expedite the development and review of certain drugs that are intended for the treatment of serious or life-threatening diseases or conditions.

Sec. 901 contains a sense of Congress that FDA should help expedite the availability of such drugs while maintaining safety and effectiveness standards. This section would require the Secretary to facilitate the development and expedite the review of a drug designated a “fast-track product” (i.e., a drug that is intended for the treatment of a serious or life-threatening disease or condition, and that demonstrates the potential to address unmet medical needs for such a disease or condition) and it enhances “accelerated approval” provisions in the FFDCA (for drugs for serious or life-threatening diseases or conditions including, but not limited to, fast-track products) by clarifying the types of evidence and endpoints on which the Secretary can rely.

Sec. 902 would require the Secretary to expedite the development and review of a drug designated a "breakthrough therapy." To achieve this designation, a drug must be intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence must indicate that it may demonstrate substantial improvement over existing therapies.

Sec. 903 would require the Secretary to ensure that opportunities exist for consultation with stakeholders from the rare disease community and to maintain a list of external scientific and medical experts to consult on products for rare diseases.

Sec. 904 would require the Architectural and Transportation Barriers Compliance Board to convene a stakeholder working group to develop best practices on access to information on prescription drug labels for individuals who are blind or visually impaired, and the GAO to study utilization of such best practices.

Sec. 905 directs the Secretary to use a consistent and systematic approach to incorporate risk-benefit into regulatory decision making and to communicate the benefits and risks of new drugs.

Sec. 906 authorizes the Secretary to contract with the National Academies of Science to conduct a study on how a prize award would incentivize innovation in all medical product development. In addition, NAS will examine how prizes would increase development of products targeted specifically for HIV/AIDS and resistant bacterial infections.

TITLE X—DRUG SHORTAGES

Current law requires sole manufacturers of certain types of drugs to notify the Secretary at least six months before discontinuing the manufacture of that drug. (The notification period may be reduced under certain conditions.) It also requires the Secretary to distribute discontinuation information to appropriate physician and patient organizations.

This title, which consists only of Sec. 1001, would amend current law by applying the notification requirement to all manufacturers of certain drugs; adding certain types of drugs, and exempting others; and requiring notification of both a permanent discontinuance and a manufacturing interruption that could lead to supply disruptions. Sec. 1001 would allow manufacturers to notify the Secretary as soon as practicable if they cannot comply with the advance notice requirement. The section would authorize the Secretary to expedite establishment inspections and review of supplements and applications that could help mitigate or prevent a "shortage," as defined in this title. The section also would require the Secretary to establish a task force to enhance the Secretary's response to shortages, and create a strategic plan to address stated aspects of shortages.

Sec. 1001 would require the Secretary, before taking an action that could lead to a supply disruption (as defined), to communicate with FDA drug shortage experts, and, if the action could reasonably cause or exacerbate a shortage, to evaluate risks of a shortage and risks associated with the FFDCA violation for which the Secretary may take action. The section also would require the Secretary to establish a mechanism for third parties to report shortages, and would mandate the Secretary's maintenance of records with specified information on shortages.

Sec. 1001 would direct the Secretary to finalize an implementing regulation within 18 months of enactment. It would authorize the Secretary to apply this section, by regulation, to biological products, although the Secretary must consider if the notification requirement for vaccines could be met through the CDC vaccine shortage notification program. Submission of a notification of a permanent discontinuance or interruption would not be construed as an admission that a product was in violation of the FFDCA or that the product was promoted or marketed for an unapproved use or indication. Sec. 1001 would require the Secretary to review regulations, guidances, policies, and practices related to drug manufacturing to identify their impacts on shortages.

Sec. 1001 would require the Secretary to clarify her position, through a guidance document, on the safe repackaging and transferring of repackaged drugs among hospitals in a common health system during a drug shortage.

TITLE XI—OTHER PROVISIONS

Sec. 1101 would reauthorize, through October 1, 2017, a sponsor's ability to receive separate approval and exclusivity for a drug containing a single enantiomer, when the racemic drug has already been approved.

Sec. 1102 would reauthorize the Critical Path Public-Private Partnerships to foster medical product innovation, authorizing the appropriation of such sums as may be necessary through FY2017.

Sec. 1111 through Sec. 1113 create an approval process for the core medical gases and mixtures of the core medical gases, which include Oxygen; Nitrogen; Nitrous Oxide; Carbon Dioxide; Helium; Carbon Monoxide; and Medical Air.

Sec. 1121 would no longer require the Secretary to seek, in making appointments to an FDA advisory committee, to reduce the likelihood that an appointed individual would later require a waiver for a potential conflict of interest. It would also eliminate the cap on the number of waivers the Secretary can grant. It would enhance recruitment and retain disclosure provisions in current law, make public the annual report regarding waivers, and require a guidance document regarding the determination that a proposed committee member has an appearance of a conflict.

Sec. 1122 would require the Secretary to issue a guidance document that describes FDA policy regarding the promotion of FDA-regulated medical products using the Internet (including social media).

Sec. 1123 would require the sponsors to electronically submit new drug applications, IND applications (but not emergency investigational new drug applications), ANDAs, BLAs, and applications for biosimilar products following issuance of a final guidance by the Secretary. This section would also require certain pre-submissions and submissions related to devices to include an electronic copy following issuance of a final guidance.

Sec. 1124 would require the Secretary to review current federal initiatives combatting prescription drug abuse to identify gaps and opportunities, and issue a report of the findings. The report will include recommendations on how to use and build upon federal data sources, disseminate best practices and develop education tools. The Secretary also must issue a guidance document within one year of enactment on the development of tamper-deterrent drug products.

Sec. 1125 would require the Secretary to make a determination concerning the labeling requirements for tanning beds within 18 months to ensure that they effectively communicate the hazards associated with heat lamp products.

Sec. 1126 would require FDA to work with other peer regulators to reduce duplication of studies necessary for premarket approval. This section does not alter the current standards for premarket review of medical products.

Sec. 1127 would require FDA to establish a strategy and implementation plan for advancing regulatory science. The report will include priorities related to medical product decision-making and regulatory and scientific gaps. FDA will report annually for FY 2013-2017 on these goals, and GAO will provide an independent assessment on the progress of the regulatory science initiatives.

Sec. 1128 would require FDA to report on a comprehensive information technology strategy plan consistent with GAO recommendations, and GAO will report on the progress of FDA to meet the goals set out in such plan.

Sec. 1129 would enhance the FDA's annual reporting requirements for medical products covered by the user fee agreements.

Sec. 1130 would require the Secretary to submit an integrated management strategy to Congress based on GAO recommendations. The plan must identify goals and priorities for CDER, CBER and CDRH and describe the actions FDA will take to develop the workforce at these centers. GAO will issue a report assessing the effectiveness of these actions toward achieving the goals and priorities in the report.

Sec. 1131 provides that elements to assure safe use included in risk management and evaluation strategies may not be used to prohibit supply of a drug to a drug developer for purposes of developing or conducting the testing necessary to support a generic drug application.