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The Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144)

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Summary

The Food and Drug Administration Safety and Innovation Act (FDASIA), P.L. 112-144, amends the Federal Food, Drug, and Cosmetic Act (FFDCA) to expand the authority of the Food and Drug Administration (FDA) in performing its human drug, biological product, and medical device responsibilities. Frequently referred to as the user fee reauthorization act, FDASIA does include four titles relating to user fees. Titles I and II reauthorize the prescription drug and medical device user fee programs (PDUFA and MDUFA). Titles III and IV authorize new user fee programs for generic drugs (GDUFA) and biosimilar biological products (BSUFA).

Title V of FDASIA reauthorizes and amends provisions of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA); it also includes other pediatric research sections. Title VI addresses the regulation of medical devices across such diverse topics as clarifying the definition of a custom device; extending for another five years the ability of the manufacturer of a humanitarian use device (one with a limited number of potential users) to make a profit on sales for pediatric use and the expansion of that ability to sales for nonpediatric use; and authorizing the Secretary of Health and Human Services to enter into arrangements with nations regarding harmonization of device regulation.

Titles VII through X address the regulation of human drugs, highlighting the areas of supply chain security, anti-infective product development incentives, expedited development and review of drugs, and drug shortages. Title XI contains a miscellany of provisions including, for example, medical gas product regulation, advisory committee conflicts of interest, and required reports and guidance from the Secretary.

For each title of FDASIA, this report provides a brief policy background narrative and an overview of provisions in P.L. 112-144. An appendix lists the time-specific requirements of federal entities in FDASIA.

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Background

The Food and Drug Administration Safety and Innovation Act (FDASIA), P.L. 112-144, continues the five-year reauthorization cycle of the prescription drug and medical device user fee programs that allow the Food and Drug Administration (FDA) to collect fees and use the revenue to support the review of brand-name drug, biological product, and device marketing applications. In addition to titles that would reauthorize the drug and device user fee programs, FDASIA includes additional titles that create new user fee authority for generic drugs and biosimilar biological products; permanently authorize programs to encourage or require studies of drugs for pediatric use; and amend the law regarding medical device regulation, drug regulation, and several areas, such as advisory committee conflict of interest, that cut across FDA product areas. Congress also made user fee reauthorizing legislation in 2007 a vehicle for addressing other FDA-related issues.[1]

Throughout the legislative process in both chambers of the 112th Congress, the chairs and ranking Members of the Senate Committee on Health, Education, Labor, and Pensions and the House Committee on Energy and Commerce expressed their intention to complete the user fee reauthorizing legislation sufficiently before the October 1, 2012, deadline to avoid disrupting FDA drug and device review staffing and activities,[2] referring to the user fee reauthorizations as must-pass legislation. **Table 1** displays the timeline of relevant committee activity.

Table 1. Committee Activity Leading to Final Passage of FDASIA (P.L. 112-144)

Action	Senate	House
Committee hearings	July, September, and November 2011; and March 2012[a]	July 2011; and February, March, and April 2012[b]
Draft bill language circulated[c]	March 16, March 29, April 4, April 17, and May 9, 2012	March 8, April 17, April 24, and May 4, 2012
Committee mark-up	S. 2516 [PCS[d]], April 25, 2012	H.R. 5651 [RH[d]], May 25, 2012
Floor passage (chamber-specific)	S. 3187 [ES[d]], May 24, 2012	H.R. 5651 [EH[d]], May 30, 2012
Floor passage (agreement)	S. 3187 [ENR[d]], June 26, 2012	S. 3187 [EAH[d]], June 20, 2012

Source: CRS compilation from committee websites and public news sources.

Notes: S. 3187, the Food and Drug Administration Safety and Innovation Act, was presented to the President on June 28, 2012, and signed by the President on July 9, 2012.

a. The Senate Committee on Health, Education, Labor, and Pensions held hearings on July 28, 2011; September 14, 2011; November 15, 2011; and March 29, 2012. The committee website has links to submitted hearing testimony (http://www.help.senate.gov/hearings/).

b. The Subcommittee on Health of the House Committee on Energy and Commerce held hearings on July 7, 2011; February 1, 2012; February 9, 2012; February 15, 2012; March 8, 2012; and April 18, 2012. The

[1] The Food and Drug Administration Amendments Act of 2007 (FDAAA, P.L. 110-85) included, along with reauthorization of prescription drug and medical device user fee programs, provisions on drug safety, direct-to-consumer drug advertising, pediatric drugs and medical devices, clinical trial databases, the creation of a new nonprofit entity to assist FDA with its mission, and food safety.

[2] The 2007 reauthorizing legislation was passed three days before the user fee authorities were to expire, thereby triggering required advance notice to staff of anticipated personnel actions.

committee website has links to submitted hearing testimony (http://energycommerce.house.gov/hearings/default.aspx).

c. See committee websites (above) for links to draft versions of legislative language.

d. The Legislative Information System (a partnership of CRS, the House, the Senate, and the Government Printing Office) uses acronyms to note different versions of a bill as it moves through the legislative process. Versions used in this table: PCS=Placed on Calendar Senate; ES=Engrossed in Senate (Passed Senate); RH=Reported in House; EH=Engrossed in House (Passed House); EAH=Engrossed Amendment House; and ENR=Enrolled Bill (Final as Passed Both House and Senate).

FDASIA has 11 titles, as listed in **Table 2**. Titles I through IV authorize FDA to collect fees and use the revenue to support specified activities for the review of prescription brand-name drugs and biological products, medical devices, generic drugs, and biosimilar biological products. Title V permanently authorizes the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act. Title VI addresses a variety of aspects of pre- and postmarket medical device regulation. Titles VII through X address the regulation of drugs, including the supply chain, antimicrobial development, expedited drug approval, and shortages. Title XI, titled Other Provisions, covers medical gas products, drug abuse, and advisory committee conflicts of interest, among other topics.

Table 2. Titles in FDASIA

Title I	FEES RELATING TO DRUGS
Title II	FEES RELATING TO DEVICES
Title III	FEES RELATING TO GENERIC DRUGS
Title IV	FEEDS RELATING TO BIOSIMILAR BIOLOGICAL PRODUCTS
Title V	PEDIATRIC DRUGS AND DEVICES
Title VI	MEDICAL DEVICE REGULATORY IMPROVEMENTS
Title VII	DRUG SUPPLY CHAIN
Title VIII	GENERATING ANTIBIOTIC INCENTIVES NOW
Title IX	DRUG APPROVAL AND PATIENT ACCESS
Title X	DRUG SHORTAGES
Title XI	OTHER PROVISIONS

Source: Food and Drug Administration Safety and Innovation Act, P.L. 112-144.

The remainder of this report presents a general overview of FDASIA by title and section, providing a narrative overview of each title, as well as a brief description of each section in the statute.[3] **Appendix A** lists the time-specific requirements of federal entities dictated by FDASIA. **Appendix B** provides a list of abbreviations and acronyms. For a comparative analysis of the provisions in the initial Senate- and House-passed versions of this legislation, see CRS Report R42564, *FDA User Fees and the Regulation of Drugs, Biologics, and Devices: Comparative Analysis of S. 3187 and H.R. 5651*, coordinated by Susan Thaul. The 14 tables in that report provide comparisons of the provisions in S. 3187 [ES] and H.R. 5651 [EH] and pre-P.L. 112-144 law.[4]

[3] The section descriptions exclude those that are not substantive, such as short titles.

[4] This report is one in a suite of CRS products that provide detailed background and analysis of FDA-related issues. For further information on many of the issues that Members and panelists raised in the committee hearings leading up to FDASIA (including drug approval, development incentives, device regulation, pediatric drugs, and user fees), see the (continued...)

Title I—Fees Relating to Drugs

FDASIA reauthorizes the prescription drug user fee program for another five years.

FDASIA reauthorizes the prescription drug user program for another five years, from FY2013 through FY2017. With the Prescription Drug User Fee Act in 1992, Congress authorized FDA to collect user fees from the manufacturers of brand-name prescription drugs and biological products and to use the revenue for specified activities.[5] PDUFA became possible when FDA, industry, and Congress agreed on two concepts: (1) *performance goals*—FDA would commit to performance goals it would negotiate with industry that set target completion times for various review processes; and (2) *use of fees*—the revenue from prescription drug user fees would be used only for activities to support the review of human drug applications and would supplement—rather than replace—funding that Congress appropriated to FDA. The added resources from user fees allowed FDA to increase staff to review what was then a backlog of new drug applications and to reduce application review times. Over the years, Congress has added similar authority regarding the regulatory review of medical devices and animal drugs.[6] User fees make up 35% of the FY2012 FDA budget. Their contribution to FDA's human drug program is larger at 51%.[7]

Following the precedent set by PDUFA, all the user fee programs addressed in this legislation include both (1) legislation and (2) performance goals agreements developed with representatives of the regulated industry in consultation with representatives of patients and advocates, academic and scientific experts, and congressional committees.

FDA may use the revenue from PDUFA fees to support "the process for the review of human drug applications."[8] With each reauthorization of PDUFA, Congress has expanded the range of activities included in that phrase. The prescription drug user fee program covers new drugs whose sponsors are the first to apply for marketing approval (excluding, therefore, generic drugs) and new biological products (excluding, therefore, the new category of biosimilar biological products).[9]

FDASIA continues the overall approach begun by the Prescription Drug User Fee Act (PDUFA) and amended by PDUFA II, III, and IV to include an annual total revenue to be equally divided

(...continued)

CRS website (the Medical Product Regulation listings are at http://www.crs.gov/pages/subissue.aspx?cliid=2678).

[5] The Prescription Drug User Fee Act (PDUFA) and its reauthorizations are in P.L. 102-571, P.L. 105-115, P.L. 107-188, and P.L. 110-85. For discussions of PDUFA, see CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): Issues for Reauthorization (PDUFA V) in 2012*, and CRS Report RL33914, *The Prescription Drug User Fee Act: History Through the 2007 PDUFA IV Reauthorization*, both by Susan Thaul.

[6] The Medical Device User Fee Act (MDUFA) and its reauthorization are in P.L. 107-250 and P.L. 110-85. The Animal Drugs User Fee Act is in P.L. 108-130, and the Animal Generic Drugs User Fee Act is in P.L. 110-316. For discussions of these user fee programs, see CRS Report R42508, *The FDA Medical Device User Fee Program*, by Judith A. Johnson, and CRS Report RL34459, *Animal Drug User Fee Programs*, by Sarah A. Lister.

[7] CRS Report R41964, *Agriculture and Related Agencies: FY2012 Appropriations*, coordinated by Jim Monke.

[8] FFDCA §735(6) [21 U.S.C. 379g (6)].

[9] For a more complete description of current law and discussion of issues relating to the Prescription Drug User Fee Act, see CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): Issues for Reauthorization (PDUFA V) in 2012*, by Susan Thaul.

among three types of fees—application, establishment, and product.[10] It also continues to define activities for which FDA can use fee revenue as those necessary for the review of human drug applications and supplements; the issuance of action letters; inspection of prescription drug establishments and other facilities; activities necessary for the review of applications for licensure of biological product establishments and for the release of lots of biologics; and monitoring of research conducted in connection with the review of human drug applications.

In general, Title I, the Prescription Drug User Fee Amendments of 2012 (commonly referred to as PDUFA V):

- Sets total fee revenue for FY2013 at $693,099,000, to be divided evenly among application fees, establishment fees, and product fees (§103).
- Continues the authority to annually adjust the total revenue allowed by inflation and workload adjustments and changes the methodology to calculate annual inflation adjustments (§103).
- Allows for the early payment of authorized fees (§103).
- To ensure that user fees supplement rather than replace congressional appropriations, continues the requirements, referred to as "triggers," that FDA may collect and use fees only if, for each year, (a) FDA spends at least as much from direct appropriations for the review of human drug applications as it had in FY1997 (adjusted for inflation), and (b) appropriations (excluding fees) for FDA salaries and expenses, overall, are equal to or greater than the appropriations (excluding fees and adjusted for inflation) for FY1997 (§103).
- Continues the requirement for annual performance and fiscal reports and adds reporting requirements (§104).
- Authorizes these prescription drug user fees from October 1, 2012, through September 30, 2017 (§§105 and 106).
- Includes a savings clause noting that fees for applications accepted by FDA for filing before October 1, 2012, will remain as under prior law (§107).

Title II—Fees Relating to Devices

FDASIA reauthorizes the medical device user fee program for another five years.

Medical devices are a wide range of products that are used to diagnose, treat, monitor, or prevent a disease or condition in a patient. For many medical devices, FDA approval or clearance must be obtained prior to marketing in the United States. Congress gave FDA the authority to collect fees from the medical device industry in 2002.[11] User fees and direct appropriations from Congress

[10] Application fee: A drug's sponsor (usually the manufacturer) must pay a fee for the FDA review each time it submits a new drug application or supplemental application, or a biologics license application. Establishment fee: Each manufacturer must pay an annual fee for each of its manufacturing establishments. Product fee: Each manufacturer must pay an annual fee for each product that fits within PDUFA's definition.

[11] MDUFMA (P.L. 107-250) added §§737 and 738 to the Federal Food, Drug and Cosmetic Act (FFDCA) [21 U.S.C. 379i and 379j]. MDUFMA was amended twice by the Medical Device Technical Corrections Act of 2004 (MDTCA; P.L. 108-214) and the Medical Device User Fee Stabilization Act of 2005 (MDUFSA; P.L. 109-43).

fund review of medical devices by the FDA. The user fees support the FDA's medical device premarket review program to help reduce the time it takes the agency to review and make decisions on marketing applications. The medical device user fee program was modeled after the PDUFA program. It provides revenue for FDA; in conjunction, the agency negotiates with industry to set *performance goals* for the premarket review of medical devices.[12]

In general, Title II, the Medical Device User Fee Amendments of 2012:

- Changes the definition of "establishment subject to a registration fee" (§202).[13]
- Changes the fee for a premarket notification submission, also called a 510(k) submission, from 1.84% of the premarket application (PMA) fee to 2% of the PMA fee; other fees are unchanged (§203).
- Sets for each fiscal year the PMA fee amounts, which start at $248,000 per application in FY2013 rising to $268,443 in FY2017, and annual establishment fee amounts, which start at $2,575 per manufacturing establishment in FY2013 rising to $3,872 in FY2016 and FY2017 (§203).
- Sets the total fee revenue amounts for each fiscal year, which start at $97,722,301 in FY2013 rising to $130,184,348 in FY2017 (§203).
- Allows for adjustment of the total revenue amounts by a specified inflation adjustment, with PMA and establishment fees adjusted accordingly (§203).
- Allows for the waiver or reduction of a PMA fee or establishment fee if that is in the interest of public health (§203).[14]
- To ensure that user fees supplement rather than replace congressional appropriations, continues the requirement, referred to as a "trigger," that FDA may collect and use fees only if the direct appropriations for devices and radiological products remain at a level (adjusted for inflation) equal to or greater than the amount specified in law (§203).[15]
- Allows for the early payment of authorized fees (§203).
- Continues the requirement for annual performance and fiscal reports and adds publication and update requirements for performance reports (§204).
- Includes a savings clause noting that fees for applications accepted by FDA for filing before October 1, 2012, will remain as under prior law (§205).
- Authorizes these medical device user fees from October 1, 2012, through September 30, 2017 (§§206 and 207).

[12] For a more complete description of the MDUFA program see CRS Report R42508, *The FDA Medical Device User Fee Program*, by Judith A. Johnson.

[13] According to FDA, this would increase the number of establishments paying the fee from 16,000 to 22,000 (MDUFA Reauthorization Public Meeting, March 28, 2012).

[14] Waivers and fee reductions must be less than 2% of total fee revenue for that year. Authority for the waiver and reduced fees would end on October 1, 2017. The fee waiver is intended for laboratory-developed test (LDT) manufacturers (MDUFA Reauthorization Public Meeting, March 28, 2012).

[15] The specified amount was changed by P.L. 112-144 from $205,720,000 to $280,587,000.

- Allows for the streamlined hiring of FDA employees to positions related to the process for the review of device applications in order to achieve performance goals (§208).[16]

Title III—Fees Relating to Generic Drugs

FDASIA authorizes a user fee program for generic drugs.

The Generic Drug User Fee Amendments (GDUFA) create new FFDCA Sections 744A, B, and C and are patterned after PDUFA, which was first enacted in 1992 and reauthorized in five-year increments. GDUFA became effective October 1, 2012, and will sunset on October 1, 2017.

Integral to the operation of the generic drug user fee program are the performance goals stated in the FDA-industry agreement that the Secretary of Health and Human Services (HHS) submitted to Congress along with proposed legislative language.[17]

In general, Title III, the Generic Drug User Fee Amendments of 2012:

- Defines "human generic drug activities" on which FDA could use revenue from GDUFA fees to include the review of generic drug submissions and related drug master files; the issuance of approval, complete response, and other letters regarding applications, supplements, and drug master files; inspections; monitoring of research; postmarket safety activities; and regulatory science activities (§302).
- Establishes three ongoing types of fees to be paid by the manufacturer: *drug master file fees* at the time of file submission*; application filing fees* (for an abbreviated new drug application [ANDA] and for a prior approval supplement [PAS] to an ANDA) at the time of submission; and annual *facility fees* (for a generic drug facility and an active pharmaceutical ingredient facility) for each establishment (§302).
- Establishes a one-time backlog fee to be paid by sponsors of currently pending applications (§302).
- Sets the estimated generic drug fee total for FY2013 at $299 million, specifies the proportion that each type of fee will contribute to the total, and provides a methodology for the calculation of an annual inflation adjustment (§302).
- To ensure that user fees supplement rather than replace congressional appropriations, sets a "trigger" by requiring that fees be refunded if appropriations for FDA salaries and expenses for a fiscal year are not at least the amount appropriated for FY2009 excluding fees for that year (§302).

[16] Streamlined hiring means hiring without regard to provisions in Title 5 of the U.S. Code. Performance goals are set forth in the Secretary's Commitment Letter. The authority to appoint such employees terminates July 9, 2015, three years after the date of enactment.

[17] For a description of that agreement and a discussion of issues relating to the Generic Drug User Fee Amendments of 2012, see CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

- Requires annual performance and fiscal reports (§§303 and 308).
- Specifies the procedure for developing recommendations for performance goals[18] in preparation for anticipated GDUFA reauthorization in 2017 (§303).
- Authorizes these generic drug user fees from October 1, 2012, through September 30, 2017 (§§304 and 305).
- Adds that a drug may be deemed misbranded (and its sale or purchase therefore prohibited) if fees and requirements of this title are not met (§306).
- Provides the Secretary with streamlined hiring authority, to expire in three years (§307).

Title IV—Fees Relating to Biosimilar Biological Products

FDASIA authorizes a user fee program for biosimilar biological products.

A biosimilar is a biological product that is highly similar to a brand-name (innovator) biological product made by a pharmaceutical or biotechnology company.[19] A biological product, or biologic, is a preparation, such as a drug or a vaccine, that is made from living organisms. In contrast to the relatively simple structure and manufacture of chemical drugs, biosimilars, with their more complex nature and method of manufacture, will not be identical to the brand-name product, but instead may be shown to be highly similar.

Biological products are, in general, regulated—licensed for marketing—under the Public Health Service Act (PHSA), and chemical drugs are regulated—approved for marketing—under the FFDCA. The Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417), often referred to as the Hatch-Waxman Act, provided a mechanism for the approval of generic chemical drugs under the FFDCA, but not for biosimilars under the PHSA.[20]

The Biologics Price Competition and Innovation Act of 2009 (BPCIA), enacted as Title VII of the Patient Protection and Affordable Care Act (ACA; P.L. 111-148), established a new regulatory authority within the FDA by creating a licensure pathway for biosimilars under the PHSA analogous to that which allowed for the approval of generic chemical drugs via the Hatch-Waxman Act under the FFDCA. Under the new pathway, a biosimilar may be approved by

[18] For a description of performance goal development and the goals associated with this GDUFA title, see CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

[19] There are no clinically meaningful differences between a biosimilar and the brand-name (also referred to as innovator) biological product in terms of the safety, purity, and potency of the product. Although a biosimilar or follow-on biologic is sometimes referred to as a biogeneric or generic biologic, the FDA and many others consider use of the word *generic* to be inaccurate because the term generic in the context of chemical drugs means identical and a biosimilar is not identical to the brand-name product. The FDA often uses the term *follow-on protein product*, because many biologics are proteins.

[20] For additional information about the Hatch-Waxman Act, see CRS Report R41114, *The Hatch-Waxman Act: Over a Quarter Century Later*, by Wendy H. Schacht and John R. Thomas

demonstrating that it is highly similar to a biological product that is already allowed on the market by FDA. The BPCIA also authorized FDA to collect associated user fees.[21]

Among other provisions, Title IV, the Biosimilar User Fee Act of 2012:

- Establishes several ongoing types of fees to be paid by the manufacturer to begin in FY2013: initial and annual biosimilar biological product development program fees for each product about which FDA holds development meetings with the sponsor; biosimilar biological product application and supplement fees at the time of submission; an annual biosimilar biological product establishment fee for each manufacturing establishment; and an annual biosimilar biological product fee for each product covered by BSUFA (§402).[22]
- Allows the fee amounts to be based, for each fiscal year, on specified proportions of the inflation-adjusted human drug application fee amount calculated (see §103) under PDUFA (§402).
- Allows for the waiver of the biosimilar biological product application fee for the first such application from a small business, defined as an entity with less than 500 employees that does not have a drug product that has been approved under a human drug application or a biosimilar biological application and introduced or delivered for introduction into interstate commerce (§402).
- To ensure that user fees supplement rather than replace congressional appropriations, sets a "trigger" by requiring that fees will be available to defray the costs of the process of review of biosimilar applications only if the Secretary allocates for such purpose $20 million, excluding fees, adjusted for inflation (§402).
- Requires annual performance and fiscal reports (§§403 and 408).

[21] For further information, see CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

[22] An initial biosimilar biological product development program fee, equal to 10% of the amount established for a human drug application, is assessed for submitting (1) a request for a biosimilar biological product development meeting, or (2) an IND application to support a biosimilar biological product application.

An annual biosimilar biological product development program fee, equal to 10% of the amount established for a human drug application, is assessed for each fiscal year following the "initial" fee unless: a marketing application for the biological product was accepted for filing; or, participation in the biosimilar biological product development program was discontinued.

A biosimilar biological product application fee is equal to the amount established for a human drug application minus the cumulative amount paid for the following fees regarding the product named in the application: initial biosimilar biological product development program fee, annual biosimilar biological product development program fee, and any reactivation fee.

A supplement fee, equal to 50% of the fee for a human drug application, is assessed for submitting a request to approve a change in a biosimilar biological product application which has been approved.

A biosimilar biological product establishment fee, equal to prescription drug establishment fee, is assessed each fiscal year for each establishment listed in an approved biosimilar biological product application that manufactures the biosimilar biological product named in the application.

A biosimilar biological product fee, equal to prescription drug product fee, is paid each fiscal year by the applicant named in the biosimilar biological product application.

- Requires an independent study of the workload volume and full costs associated with the review of biosimilar biological product applications (§403).
- Specifies the procedure for developing recommendations for performance goals[23] in preparation for anticipated BSUFA reauthorization in 2017 (§403).
- Authorizes these biosimilar user fees from October 1, 2012, through September 30, 2017 (§§404 and 405).
- Includes a savings clause noting that fees for applications accepted by FDA for filing before October 1, 2012, will remain as under prior law (§406).

Title V—Pediatric Drugs and Devices

FDASIA permanently authorizes the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act.

Drug manufacturers may be reluctant to test drugs and medical devices in children because of economic, ethical, legal, and other obstacles.[24] The Best Pharmaceuticals for Children Act (BPCA, P.L. 107-109)[25] and the Pediatric Research Equity Act (PREA, P.L. 108-155)[26] provided drug manufacturers financial and regulatory incentives to test their products for use in children. The Pediatric Medical Device Safety and Improvement Act of 2007 (PMDSIA, P.L. 110-85) created reporting requirements for pediatric medical devices and incentives for manufacturers to create pediatric medical devices, and gave FDA the authority to require postmarket studies of approved pediatric devices to ensure their continued efficacy and safety.

BPCA and PREA, passed by Congress in 2002 and 2003 and subsequently reauthorized in 2007, represent Congress's attempt to address the need for pediatric testing of drugs and biologics. BPCA created an incentive (extended market exclusivity) for manufacturers to conduct studies on pediatric use, and PREA created a requirement for manufacturers to test the safety and effectiveness of their products in pediatric populations. Between September 27, 2007, and March 31, 2012, 369 studies were completed under BPCA, PREA, or both.[27] BPCA and PREA were again reauthorized in FDASIA.

[23] For a description of performance goal development and the goals associated with this BSUFA title, see CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

[24] CRS Report RL33986, *FDA's Authority to Ensure That Drugs Prescribed to Children Are Safe and Effective*, by Susan Thaul.

[25] The FDA Modernization Act of 1997 (FDAMA, P.L. 105-115) provided an incentive in the form of a six-month extension of marketing exclusivity to drug manufacturers that completed pediatric studies requested by the FDA. The FDA would not approve the sale of another manufacturer's product during that period. In 2002, Congress passed BPCA, which reauthorized this program for five years. In 2007, the FDA Amendments Act of 2007 (FDAAA, P.L. 110-85) reauthorized the program for another five years. FDASIA permanently authorized the program.

[26] In 1998, FDA published a rule, known as the Pediatric Rule, which required manufacturers to submit pediatric testing data at the time of all new drug applications. In 2002, a federal court struck down the rule, holding that FDA lacked the statutory authority to promulgate it. Congress gave FDA that authority with PREA. PREA covers drugs and biological products and includes provisions for deferrals and waivers.

[27] FDA, "Breakdown of FDAAA Completed Pediatric Studies," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm190622.htm.

Extended marketing exclusivity may be an attractive incentive to a manufacturer with a product that is being sold under patent or other types of exclusivity protections.[28] BPCA also included provisions to refer pediatric studies of off-patent products, which no longer have market exclusivity, to the National Institutes of Health (NIH), and manufacturer-declined studies of on-patent products to the Foundation for the NIH.[29]

BPCA and PREA studies result in information on new dosing, new indications of use, new safety information, and new data on effectiveness that inform labeling changes for pediatric dosing, warnings, and instructions on how to prepare formulations for pediatric populations. Although BPCA and PREA were developed separately, they are usually discussed in tandem because they both relate to pediatric research and PREA's continuity has been linked to the BPCA market exclusivity authority.

In general, Title V:

- Permanently authorizes BPCA and PREA (§501).
- Clarifies the Secretary's authority to award exclusivity for studies conducted under PREA if they are completed and accepted pursuant to a written request under BPCA; and requires the Secretary to provide an explanation if a written request does not include the study of neonates (§502).
- Requires the Secretary to issue standard operating procedures for Pediatric Review Committee review of specified study plans and written requests under BPCA and PREA (§503).
- Requires that the Secretary make available for the public the medical, statistical, and clinical pharmacology reviews of (and agency requests for) studies submitted between January 4, 2002, and September 27, 2007, under BPCA that resulted in six months of market exclusivity and a labeling change (§504).
- Allows extensions of study deferrals under specified conditions; sets timeframes for deferral requests and Secretarial responses; requires the Secretary to track and make information on deferrals and deferral extensions available to the public; and allows the Secretary to enforce assessment deadlines and to consider a drug or biological product misbranded for failure to submit a required assessment, but not to withdraw drug approval or to revoke biologics licensure (§505).
- Provides timeline and specifies content for a sponsor's required initial study plan submission (no later than 60 days after the end of Phase 2), and subsequent steps by the sponsor and the Secretary (§506).
- Permanently authorizes the Pediatric Advisory Committee for specified activities; authorizes the Pediatric Subcommittee of the Oncologic Drug Advisory Committee for the duration of the committee; and authorizes appropriations of

[28] The FFDCA authorizes marketing exclusivity in specified circumstances for pediatric studies, orphan drugs, new chemicals, and patent challenges. FDA, "Frequently Asked Questions on Patents and Exclusivity," http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079031.htm.

[29] FNIH, established by Congress in 1990, is an independent non-profit organization that works "raising private funds and creating public-private partnerships to support the mission of the NIH" (FNIH, "About the Foundation for NIH," http://www.fnih.org/about).

$25 million for each of FY2013 through FY2017 for the program for the study of off-patent drugs at NIH (§507).

- Extends until October 1, 2017, the waiver of the prohibition on the sale for profit of certain pediatric devices that are approved under the humanitarian device exemption from required effectiveness data (§507).
- Requires reports, with specified content and to include stakeholder input, to committees of jurisdiction and the public within four years and every five years thereafter (§508).
- Makes technical amendments (§509).
- Requires the Secretary to hold a meeting and report on a strategic plan on accelerated development of new therapies for pediatric rare diseases (§510).
- Adds expertise in a pediatric subpopulation, neonatology, and pediatric epidemiology to the areas required to be represented on the staff of the Office of Pediatric Therapeutics (§511).

Title VI—Medical Device Regulatory Improvements

FDASIA makes modifications to various aspects of premarket and postmarket device regulation.

Medical devices include a wide range of products that are used to diagnose, treat, monitor, or prevent a disease or condition in a patient. Medical devices are broadly integrated into health care and include simple devices, such as tongue depressors, as well as more complex devices, such as implantable hips. The extent of FDA authority to regulate whether a device may be marketed in the United States and how it is monitored afterward varies across types of devices.[30]

In order to determine the applicability of premarket requirements (i.e., clearance or approval before marketing) for a given device, FDA classifies the device based on the risk to the patient: (1) low-risk devices are class I; (2) moderate-risk are class II; and (3) high-risk are class III. Low-risk medical devices (class I) and a very small number of moderate-risk medical devices (class II) are exempt from premarket review. In general, for moderate-risk and high-risk medical devices, there are two pathways that manufacturers can use to bring such devices to market with FDA's permission: (1) premarket approval (PMA) and (2) premarket notification submission (also known as a 510(k) submission, after the section in the FFDCA that authorized this type of notification).

The PMA process generally consists of conducting clinical studies and submitting a PMA application, which requires evidence providing reasonable assurance that the device is safe and effective. This is somewhat analogous to the new drug application process. A PMA is used for novel and high-risk devices, is often lengthy and expensive, and results in a type of FDA permission called approval. The other path involves submitting a 510(k) notification demonstrating that the device is substantially equivalent to a device already on the market (a predicate device) that does not require a PMA. The 510(k) process is unique to medical devices

[30] For additional information, see CRS Report R42130, *FDA Regulation of Medical Devices*, by Judith A. Johnson.

and results in FDA clearance. Substantial equivalence is determined by comparing the performance characteristics of a new device with those of a predicate device.

Once a device is on the market, FDA has authority to carry out certain activities to monitor its safety and effectiveness. The extent of the agency's postmarket authority is tied to characteristics of the device. Manufacturer requirements include areas such as labeling, postmarket surveillance, device tracking, and adverse event reporting.

Provisions in FDASIA make modifications to various aspects of premarket and postmarket device regulation. Premarket modifications include those intended to (1) affect the efficiency, transparency, and data requirements of the 510(k) and PMA processes; and (2) alter or make clarifications to certain types of exempt devices, for example, custom devices and humanitarian use devices. With respect to postmarket regulation, provisions focus on expanding active postmarket surveillance; altering requirements related to postmarket studies for devices; and strengthening both device recall and tracking capabilities through a recall program and the unique device identifier system. Miscellaneous reforms include those aimed at increasing transparency of FDA's approval and clearance decisions and processes for issuing industry guidance documents; improving health information technology for the agency; and harmonizing device regulation with FDA's international counterparts.

In general, Title VI:

- Clarifies that the Secretary will not be allowed to disapprove an investigational device exemption (IDE) application[31] because the Secretary determines that (1) the investigation may not support a substantial equivalence or de novo classification determination[32] or approval of a device, (2) the investigation may not meet a requirement, including a data requirement, relating to the approval or clearance of a device, or (3) an additional or different investigation may be necessary to support clearance or approval of the device (§601).
- To clarify "the least burdensome standard" for PMA applications (without altering the criteria for evaluating a PMA application), defines the requirement for necessary clinical data as the minimum required to demonstrate, for purposes of approval, the effectiveness of a device for the conditions of use (§602).
- To clarify "the least burdensome standard" for 510(k) notifications (without altering the standard for determining substantial equivalence), defines the requirement for necessary information (to demonstrate that devices with differing technological characteristics are substantially equivalent) as the minimum required to support a determination of substantial equivalence between a new device and a predicate device (§602).

[31] Clinical evaluations of investigational devices must have an investigational device exemption (IDE) before the study is initiated. An IDE allows an unapproved device (most commonly an invasive or life-sustaining device) to be used in a clinical study to collect the data required to support a PMA application.

[32] Under the FFDCA, novel devices lacking a legally marketed predicate are automatically designated class III. A provision in FDAMA of 1997 allowed FDA to establish a new, expedited mechanism for reclassifying these devices based on risk, thus reducing the regulatory burden on manufacturers. The "De Novo Classification Process" allows FDA to reclassify a novel low- to moderate-`risk device into class I or II.

- Requires the Secretary to completely document the scientific and regulatory rationale for any significant decision regarding submission or review of a report under Section 510(k), a PMA application, or an IDE application, including documentation of significant controversies or differences of opinion, and to provide this documentation to the applicant upon request; a supervisory review of the significant decision may also be requested (§603).
- Requires the Secretary to withdraw the July 2011 draft FDA guidance entitled "Guidance for Industry and FDA Staff—510(k) Device Modifications: Deciding When to Submit a 510(k) for a Change to an Existing Device," leaving the prior guidance issued in 1997 in effect (§604).
- Requires a report to House and Senate committees regarding when a 510(k) notification should be submitted for a modification or change to a legally marketed device; draft guidance or proposed regulation on 510(k) device modification will not be issued before these committees receive this report and final guidance or regulation will not be issued until one year after the committees receive such report (§604).
- Requires the Secretary to establish a program to improve the device recall system, to include the assessment of information on device recalls; clarification of procedures for conducting device recall audit checks; assessment of the effectiveness of corrections or action plans for recalls; and documentation of the basis for terminations of recalls (§605).
- Allows the Secretary, at any time, to issue a clinical hold prohibiting the sponsor of a medical device from conducting a clinical investigation using the medical device if the Secretary determines the device represents an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation or for such other reasons the Secretary may establish by regulation (§606).
- Allows the Secretary, for certain new devices, in response to a request for an initial device (de novo) classification, to classify the new device without first issuing a determination that it is not substantially equivalent (NSE) to an existing device; this classification request may be declined if there exists a legally marketed device on which to base a substantial equivalence review, or if the new device is not a low-moderate risk device or general controls would be inadequate to control risks and special controls cannot be developed (§607).
- Allows the Secretary to change the classification of a device based on new information, and to revoke any regulation or requirement under FFDCA Sections 514 or 515, by *administrative order* instead of by regulation; requires publication of the proposed order with a substantive summary of the scientific evidence for the reclassification; specifies requirements for public comment, a meeting of a device classification panel, and a final order; specifies that Administrative Procedure Act requirements regarding regulations would not apply, although the order would be subject to judicial review; and limits authority to issue the administrative order so it cannot be delegated below the Director of the Center for Devices and Radiological Health, acting in consultation with the FDA Commissioner (§608).
- Authorizes the Secretary, with respect to devices, to enter into arrangements with nations regarding harmonization of regulatory requirements for activities,

including inspections and common international labeling symbols, and to participate in international fora, including the International Medical Device Regulators Forum (§§609 and 610).

- Reauthorizes, through October 1, 2017, the inspection of a factory, warehouse, or manufacturing or processing establishment by accredited third parties, and reauthorizes, through October 1, 2017, the review of 510(k) submissions by accredited third parties and establishes criteria for periodic reaccreditation (§§611 and 612).
- Allows a device granted a humanitarian device exemption (HDE)[33] to qualify for an exemption to the general ban on selling such devices for a profit if the HDE device is intended for the treatment or diagnosis of (1) a disease or condition that does not occur in pediatric patients, or, (2) that occurs in pediatric patients in such numbers that device development is impossible, highly impracticable, or unsafe (§613).
- Allows a sponsor of a device granted an HDE prior to the bill's enactment to seek a determination as to whether it would qualify for an exemption to the profit ban (§613).
- Requires the Secretary to issue proposed regulations for a unique device identification system not later than December 31, 2012; to finalize proposed regulations no later than 6 months after the close of the comment period; and to implement final regulations with respect to certain devices no later than two years after finalization of the regulations (§614).
- Requires the Secretary to modify Sentinel (the Postmarket Risk Identification and Analysis System) to include medical devices, and requires the Secretary, when expanding this system, to engage stakeholders and to use relevant data on cleared and approved devices (§615).
- Specifies that the Secretary's authority to order the conduct of postmarket surveillance is at the time of approval or clearance of a device or at any time thereafter; and requires the manufacturer to commence any required postmarket surveillance not later than 15 months after being so ordered (§616).
- Broadens the definition of custom devices, which are exempt from the requirements of FFDCA Sections 514 and 515; outlines limitations to the exemption; and requires the Secretary to promulgate regulations on the replication of custom devices (§617).
- Requires the Secretary to make public a report containing a proposed strategy and recommendations on a regulatory framework pertaining to health information technology, including mobile medical applications, and authorizes

[33] The Safe Medical Devices Act of 1990 (P.L. 101-629) authorized the HDE to encourage the development of devices that aid in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States per year. An HDE application is similar to a PMA, but exempt from the effectiveness requirements. However, there are some important restrictions, including that the device sponsor may not make a profit on the sale of the device if its price is more than $250. FDAAA (P.L. 110-85) removed the restriction on profits for HDEs developed for pediatric use.

the Secretary to convene a working group of external stakeholders to provide input on the strategy and recommendations required in this report (§618).

- Treats three types of notices related to devices as guidance documents for the purposes of ensuring that procedural requirements on public participation would apply to such documents (unless the Secretary determines participation is not feasible or appropriate) before they could be implemented: (1) notice to industry guidance letters; (2) notice to industry advisory letters; and (3) notices setting forth either initial interpretations of a regulation or policy or changes in interpretation or policy (§619).
- Reauthorizes the Improving Pediatric Device Availability Demonstration Grants, allowing an appropriation of $5.25 million for each of FY2013 through FY2017, and requires a rule regarding the tracking of pediatric uses of devices be proposed by December 31, 2012, and the final rule be implemented by December 31, 2013 (§620).

Title VII—Drug Supply Chain

FDASIA expands FDA authority regarding manufacturer registration, facility inspection, and importation.

FDA's earliest authorities, in 1906, concerned product integrity. Subsequent changes in the law related to integrity and safety reflected the mid-century pharmaceutical industry with mostly domestic factories. As drug production has shifted to a global supply chain of manufacturers, processers, packagers, importers, and distributors, FDA leadership, among others, has suggested that the agency's statutory authority does not match its responsibilities.[34] FDASIA responds, in part, with provisions to allow FDA to refuse entry of an imported drug if the manufacturing facility inspection was denied or limited; enhance penalties for suppliers of counterfeit or substandard products; and require a unique manufacturing facility identifier. Despite discussions right up to FDASIA enactment, Congress did not reach agreement on language regarding other items, such as chain-of-custody documentation and track-and-trace technologies. Following FDASIA passage, Members have continued such discussions, attempting to find an effective and feasible mix that covers domestic and foreign facilities.[35]

In general, Title VII, Drug Supply Chain:

- Expands the registration information required from the owners or operators of domestic and foreign drug establishments to include a unique facility identifier and information about importers (§§701 and 702).

[34] Statement of Deborah M. Autor, Esq., Deputy Commissioner for Global Regulatory Operations and Policy, FDA, before the Senate Committee on Health, Education, Labor, and Pensions, "Securing the Pharmaceutical Supply Chain," September 14, 2011, http://www.fda.gov/NewsEvents/Testimony/ucm271073.htm; and statement of Janet Woodcock, M.D., Director, FDA Center for Drug Evaluation and Research, before the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, "FDA's Ongoing Heparin Investigation," April 29, 2008, http://www.fda.gov/NewsEvents/Testimony/ucm115242.htm.

[35] "As Congress Continues to Mull Track and Trace, California Plows Ahead on ePedigree," *Drug Industry Daily*, August 3, 2012.

- Expands registration information required to include establishments that manufacture excipients (such as fillers, preservatives, and flavors) for listed products (§703).
- Requires the Secretary to maintain an electronic database of unique facility identifiers (§704).
- Requires the Secretary to carry out biennial inspections of establishments that manufacture class II or class III devices (§705).
- Requires the Secretary to carry out manufacturing establishment inspections according to a risk-based schedule for both prescription and nonprescription drugs; specifies risk factors and requires reports (§705).
- Requires manufacturers to submit required records in advance or in lieu of inspections within a reasonable timeframe; and requires the Secretary to sufficiently describe the records requested and to provide receipt confirmations (§706).
- Requires that a drug be deemed adulterated if the owner or operator of a facility used in its manufacture delays, denies, or limits an inspection, or refuses to permit entry or inspection (§707).
- Allows the Secretary to destroy an adulterated, misbranded, or counterfeit drug offered for import if it is valued at $2,500 or less; and includes language about notice, storage, cost liability, and regulations (§708).
- Expands the Secretary's authority to administratively detain a product found to be adulterated or misbranded during a facility inspection to include drugs (prior authority was for device and tobacco products) (§709).
- Allows the Secretary to, in specified conditions, keep confidential the information relating to drug inspections that a foreign government provided voluntarily (§710).
- Notes that, with respect to the criteria for deeming a drug to be adulterated, "current good manufacturing practices" include quality controls in manufacturing, and assurance of the safety of raw materials (§711).
- Allows the Secretary to enter into agreements with foreign governments to recognize inspections of foreign establishments in specified situations (§712).
- Allows the Secretary to require, as a condition of granting a drug admission to the United States, an importer to provide specified information demonstrating that the drug complies with requirements of this act (§713).
- Requires a commercial importer to register with the Secretary and submit, among other things, a unique facility identifier; requires the Secretary to promulgate regulations to establish good importer practices; and prohibits the importation of drugs by unregistered commercial importers (§714).
- Allows the Secretary to require that a registered manufacturer, a wholesaler, or a distributor (other than for retail sale) notify the Secretary when that person knows (1) that the use of a drug may result in serious illness or death; (2) of a significant theft of such drug; or (3) of the counterfeiting of such drug that is in U.S. commerce or could be imported (§715).

- Requires imprisonment for up to 20 years or a fine up to $1 million for a person who knowingly and intentionally adulterates a drug so that the drug has a reasonable probability of causing serious adverse health consequences or death to humans or animals (§716).
- Adds trafficking in a counterfeit drug to the list of violations subject to fines and imprisonment under the U.S. criminal and penal code, and directs the U.S. Sentencing Commission to amend guidelines to increase penalties to reflect the serious nature of these offenses (§717).
- Asserts U.S. authority to enforce the FFDCA for a violation that occurs outside the United States if the product was intended for U.S. import or if an act committed in the United States furthers the violation (§718).

Title VIII—Generating Antibiotic Incentives Now

FDASIA provides incentives for the development of certain new anti-infective drugs.

The treatment of infectious diseases often depends on the availability of anti-infective drugs. Approved drugs can become ineffective if infectious organisms develop resistance to them. However, development of new anti-infective drugs is not always attractive to sponsors; the drugs are often used short-term and/or in small numbers of patients, compared with so-called "blockbuster" drugs.[36] In addition, some drug companies cited unique regulatory challenges in the approval of anti-infective drugs.

FDASIA provides incentives for the development of certain new anti-infective drugs by providing an extended period of exclusivity (i.e., a period in which the new drug may be marketed without generic competition). This and other provisions, summarized below, are modified from the freestanding Generating Antibiotic Incentives Now Act of 2011 (GAIN Act), S. 1734/H.R. 2182.

In general, Title VIII:

- Defines a *qualified infectious disease product* (QIDP) as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections (§801).
- Requires the Secretary to determine whether a product is a QIDP within 60 days of a sponsor's request (§801).
- Provides, for a QIDP, five years of market exclusivity, in addition to other periods of exclusivity for which such drug qualifies (§801).
- Requires the Secretary to finalize implementing regulations within two years of enactment (§801).
- Makes QIDPs eligible for priority review and designation as fast track products[37] (§§802 and 803).

[36] A "blockbuster" drug is commonly defined as one that is in widespread use and that generates at least $1 billion in annual sales.

[37] For information about these expedited review procedures, see CRS Report RS22814, *FDA Fast Track and Priority* (continued...)

- Requires the Secretary to update guidance documents regarding the conduct of clinical trials for antibacterial and antifungal drugs; and to provide written recommendations for such trials upon a sponsor's request (§804).
- Requires the Secretary, within five years of enactment, to report to Congress on specified aspects of the implementation of this title (§805).
- Requires the Secretary, by June 30, 2013, to publish draft guidance on the development of drugs to treat serious or life-threatening bacterial infections; and to finalize such guidance by December 31, 2014 (§806).

Title IX—Drug Approval and Patient Access

FDASIA augments tools to expedite the development and review of drugs for serious or life-threatening conditions.

Before a drug may be sold in the United States, FDA must approve an application from its manufacturer. The progression to drug approval begins before FDA involvement as, first, basic scientists work in the laboratory and with animals, and, second, a drug or biotechnology company develops a prototype drug. That company must seek and receive FDA approval, by way of an investigational new drug (IND) application, to test the product with human subjects. Those tests, called clinical trials, are carried out sequentially in Phase I, II, and III studies, which involve increasing numbers of subjects. The manufacturer then compiles the resulting data and analysis in a new drug application (NDA). FDA reviews the NDA with three major concerns: (1) safety and effectiveness in the drug's proposed use; (2) appropriateness of the proposed labeling; and (3) adequacy of manufacturing methods to assure the drug's identity, strength, and quality. The FFDCA and associated regulations detail requirements of each step; not all reviews and applications follow the standard procedures.

In certain circumstances, FDA regularly uses three formal mechanisms to expedite the development and review process.[38] For a drug for a serious or life-threatening condition, *accelerated approval*[39] and *animal efficacy approval*[40] processes—provided for in regulations—change what is needed in an application when a drug or biological product may provide a meaningful therapeutic benefit over existing treatments. For a drug intended to treat a serious or life-threatening condition that demonstrates the potential to address an unmet medical need, a *fast track product* designation[41]—provided for in law—allows approval of an application based on the

(...continued)

Review Programs, by Susan Thaul.

[38] For a discussion of drug development and the Food and Drug Administration (FDA) review process, including these special mechanisms, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by Susan Thaul.

[39] 21 CFR 314 Subpart H for drugs, and 21 CFR 601 Subpart E for biological products. A second accelerated approval situation addresses drugs whose use FDA considers safe and effective only under set restrictions that could include limited prescribing or dispensing. FDA usually requires postmarketing studies of products approved this way.

[40] The Animal Efficacy Rule allows manufacturers to submit effectiveness data from animal studies as evidence to support applications of certain new products "when adequate and well-controlled clinical studies in humans cannot be ethically conducted and field efficacy studies are not feasible" (21 CFR 314 Subpart I and 21 CFR 601 Subpart H).

[41] FFDCA §506 [21 U.S.C. §356]. FDA, "Guidance for Industry: Fast Track Drug Development Programs—Designation, Development, and Application Review," Center for Drug Evaluation and Research and Center For Biologics Evaluation and Research, January 2006.

product's "effect on a clinical endpoint or on a surrogate endpoint that is reasonably likely to predict clinical benefit." *Priority review*—based in FDA procedures—affects the timing of the review, not the process leading to submission of an application, when FDA determines a drug would address an unmet need.[42]

Provisions in FDASIA amend the FFDCA to "help expedite the development and availability to patients of treatments for serious or life-threatening diseases or conditions while maintaining safety and effectiveness standards."[43] They do so by combining elements of the regulatory *accelerated approval* process and the statutory *fast track product* designation, and creating a new designation—*breakthrough therapy*—for a drug whose preliminary clinical data suggest a possible substantial improvement over existing therapies.

In general, Title IX:

- Requires the Secretary, at the request of a sponsor, to facilitate the development and expedite the review of a drug designated a *fast track product*, if the drug "is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a condition" (§901).
- Designates an *accelerated approval* process by which the Secretary may approve a marketing application of a product for a serious or life-threatening disease or condition, including (but not limited to) a fast track product, based upon a clinical or surrogate endpoint that, among other specified criteria, "is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit" (§901).
- Authorizes the Secretary to require postmarket activities, expedite withdrawal of approval, facilitate review, and contract for an independent evaluation of the various expedited approval processes; requires the Secretary to issue guidance and amend regulations; does not alter the standards of evidence of safety and effectiveness required for drug approval; and does not alter the Secretary's ability to use evidence from other than adequate and well-controlled investigations in order to determine whether an endpoint is reasonably likely to predict clinical benefit (§901).
- Requires the Secretary, upon request of a sponsor, to expedite the development and review of a drug designated a *breakthrough therapy*, "if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints"; requires the Secretary to submit annual reports to Congress on the number of requested and approved breakthrough therapy designations and related actions; and establishes timeframes for related guidance (§902).

[42] FDA, "Fast Track, Accelerated Approval and Priority Review," http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm.

[43] Sense of Congress, §901(a) of P.L. 112-144.

- Requires the Secretary to develop and disseminate to appropriate persons and organizations a description of the law applicable to accelerated approval, fast track, and breakthrough products; and establish a program to encourage the development of "surrogate and clinical endpoints, including biomarkers, and other scientific methods and tools that can assist the Secretary in determining whether the evidence submitted in an application is reasonably likely to predict clinical benefit" for serious or life-threatening conditions with significant unmet medical needs (§§901 and 902).
- With regard to new drugs and biological products for rare diseases, and drugs and biological products that are genetically targeted, requires the Secretary to (1) ensure that opportunities exist for consultations with stakeholders and (2) develop and maintain a list of external experts with whom to consult when the Secretary lacks the requisite expertise; specifies topics for such consultations (§903).
- Requires 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; requires a GAO study of the extent to which pharmacies use those best practices and the extent to which barriers to accessible information continue (§904).
- Requires the Secretary to "implement a structured risk-benefit assessment framework in the new drug approval process," without altering premarket approval evaluation criteria (§905).
- Reauthorizes the appropriation of $30 million for each of FY2013 through FY2017 for grants and contracts to defray the costs of qualified testing used for orphan drug development; and eliminates a requirement in the Orphan Drug Act that, in order to qualify, such costs must be incurred *after* designation as a drug for a rare disease or condition (§906).
- Requires the Secretary to publish on the FDA website and provide to Congress a report, with specified content, addressing the extent to which demographic subgroups (to include sex, age, race, and ethnicity) participate in clinical trials and are included in safety and effectiveness data submitted in marketing applications; and to publish an action plan with recommendations to improve the completeness, quality, and inclusion of subgroup data in various analyses (§907).
- Creates a new program, funded by user fees, to provide a transferable voucher, under specified conditions, to a sponsor of an approved new drug or biological product for a rare pediatric disease to be used for the priority review of another application; terminates the authority to award such vouchers one year after the Secretary awards the third rare pediatric disease priority voucher; and requires the GAO to report on the effectiveness of the program (§908).

Title X—Drug Shortages

FDASIA expands requirements for manufacturers, the Attorney General, and the Secretary toward preventing and mitigating shortages.

Since 2005, FDA, clinicians, pharmacists, and patients have noted more frequent drug shortages (i.e., when the local or nationwide supply of a particular dosage is inadequate to meet demand). Recent shortages have clustered around generic sterile injectable drugs used during surgery or hospital care, although shortages have affected brand-name products and oral tablets for a wide range of diseases and conditions.[44]

Immediate causes of shortages include (1) manufacturing quality problems (such as contaminants); (2) interruption in supply of ingredients; (3) unanticipated increase in demand (e.g., the unavailability of another product for the same condition, recent attention to an off-label use, or approval of an additional indication or user population); (4) business decisions by individual firms (e.g., to cut back on the number of facilities dedicated to a particular drug, or to shut down during renovation); and (5) unanticipated weather, accident, or other event.[45] Less clear is why the rate of shortages is increasing now. Market concentration and a global supply chain, along with manufacturing capacity constraints, the complex process of drug production, inventory practices, and pricing, act as underlying causes, many believe, of drug shortages.[46]

FDA has acted within its current authority by asking both sole source manufacturers and other firms to increase production; exercising flexibility through regulatory discretion (e.g., allowing the importation of certain drugs); expediting review; and communicating with the Drug Enforcement Administration (DEA) about increasing quotas of controlled substances that are in short supply.[47] An October 2011 executive order directed FDA to use all tools to require that manufacturers give advance notice of manufacturing interruptions, to expedite applications, and to work with the Department of Justice (DOJ) to address instances of price gouging, for example, when pharmacies turn to supplies outside their routine distribution channels.[48] FDA and GAO analyses suggested immediate steps to increase notification, increase staffing, develop legislation to require notification, and communicate with the public and within FDA. They suggested longer-term steps such as using databases to identify factors that help prevent or mitigate shortages, identifying manufacturing quality issues and having backup plans, using sentinel reports from providers to identify imminent shortages, and encouraging wholesaler transparency.[49] Provisions

[44] FDA, "Current Drug Shortages," http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm.

[45] FDA, "A Review of FDA's Approach to Medical Product Shortages," October 31, 2011, http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf; and Government Accountability Office (GAO), "Drug Shortages: FDA's Ability to Respond Should Be Strengthened," Report to Congressional Requesters, GAO-12-116, November 2011, http://gao.gov/assets/590/587000.pdf.

[46] Department of Health and Human Services (HHS), "Economic Analysis of the Causes of Drug Shortages," ASPE Issue Brief, Office of Science and Data Policy, Office of the Assistant Secretary for Planning and Evaluation, October 2011, http://aspe.hhs.gov/sp/reports/2011/DrugShortages/ib.pdf.

[47] FDA, "A Review of FDA's Approach to Medical Product Shortages," October 31, 2011, http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM277755.pdf.

[48] The White House, "Executive Order 13588—Reducing Prescription Drug Shortages," Office of the Press Secretary, October 31, 2011, http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-13588-reducing-prescription-drug-shortages.

[49] Some Members of Congress have considered other approaches, such as requiring pedigrees and data systems to both (continued...)

in FDASIA reflect some of the items in the executive order and in the GAO and FDA recommendations.

In general, Title X:

- Expands the requirement that a manufacturer of certain drugs notify the Secretary of a permanent discontinuance of its production to include a broader range of drugs and an *interruption* in production; describes secretarial actions when a manufacturer fails to meet the requirements; authorizes the Secretary to expedite an inspection or the review of a supplemental application to help mitigate or prevent a shortage; addresses Attorney General actions regarding increasing the production quota of a controlled substance to address a shortage; and addresses procedures and regulations (§1001).
- Requires the Secretary to submit annual reports to Congress to include the number of actual and prevented shortages and manufacturer notifications, FDA communication procedures, specified details of FDA shortage prevention and mitigation actions, and efforts to coordinate with DEA (§1002).
- Requires the Secretary to establish a task force to develop and implement a strategic plan regarding the Secretary's response to preventing and mitigating shortages; describes required elements of the strategic plan, including considering whether to establish a qualified manufacturing partner program; and specifies other communication and action requirements (§1003).
- Requires that the Secretary maintain an up-to-date list, with specified information, of drugs that the Secretary determines to be in shortage in the United States and make the information publicly available except when the Secretary determines that the disclosure would adversely affect the public's health or the information is protected as a trade secret or confidential information elsewhere in the U.S. Code (§1004).
- Requires the Attorney General, upon a request from a manufacturer of a schedule II controlled substance listed as in shortage, to increase the production quota or provide the reason for denial and requires the Secretary to make the manufacturer's written request available to the public (§1005).
- Requires the Attorney General to submit to Congress an annual drug shortages report with specified content relating to controlled substances (§1006).
- Excludes from the establishment registration requirement a hospital that repackages a drug on the FDA drug shortage list for transfer to another hospital in the same health system (§1007).
- Requires GAO to "examine the cause of drug shortages and formulate recommendations on how to prevent or alleviate such shortages," specifying questions to consider, and to submit to Congress a report on the study results (§1008).

(...continued)

track the availability and verify the legitimacy of shipments; providing incentives to manufacturers; or exploring whether reimbursement and purchasing policies for Medicare, Medicaid, other public programs may contribute to drug shortages.

Title XI—Other Provisions

FDASIA includes 31 other provisions that address reauthorizations, medical gas regulation, advisory committee conflict of interest, and synthetic drug regulation, among other things.

Subtitle A—Reauthorizations

In general, Subtitle A—Reauthorizations:

- Extends, until October 1, 2017, the period during which a manufacturer may elect to consider a non-racemic drug as a separate drug from an approved racemic (having both the left- and right-handed molecular forms of an active ingredient) drug with the same active ingredient and changes the restriction on using any investigations of the racemic drug in support of the non-racemic drug's application to restrict only the use of clinical investigations (§1101).
- Reauthorizes the Critical Path Public-Private Partnerships, through which FDA can enter into collaborative agreements with eligible educational or tax-exempt organizations to foster medical product innovation, development, and safety; and authorizes the appropriation of $6 million for each of FY2013 through FY2017 (§1102).

Subtitle B—Medical Gas Product Regulation

Subtitle B addresses the regulation of medical gases, such as oxygen. Although they are considered to be prescription drugs under the FFDCA, FDA has exercised regulatory discretion in not requiring new drug applications or imposing user fees on medical gas manufacturers. However, these companies sought an approval pathway in law to avoid certain trade and other problems associated with their products being considered "unapproved." FDASIA allows the Secretary to approve medical gases that meet requirements through a certification process that would not confer market exclusivity or require the payment of user fees.

In general, Subtitle B—Medical Gas Product Regulation:

- Establishes a process requiring the Secretary, within 180 days of enactment, to certify certain medical gas products that meet specified requirements; considers a certified product to have an approved drug application for specified indications, but without eligibility for market exclusivity or the requirement to pay prescription drug user fees; and authorizes the Secretary to waive requirements for a prescription (§1111).
- Requires the Secretary to review and report on current medical gas regulations within 18 months of enactment; amend them as needed; and finalize them within 48 months of enactment (§1112).
- Clarifies that this subtitle would not apply to medical gases that were approved prior to enactment, or that are approved after enactment, pursuant to typical drug approval authority (§1113).

Subtitle C—Miscellaneous Provisions

In general, Subtitle C—Miscellaneous Provisions:

- Requires the Secretary, within two years of enactment, to issue a guidance document that describes FDA policy regarding the promotion of FDA-regulated medical products using the Internet, including social media (§1121).
- Requires the Secretary to "review current federal initiatives and identify gaps and opportunities with respect to … ensuring the safe use of prescription drugs with the potential for abuse [and] the treatment of prescription drug dependence"; post on the HHS website a report on the findings of the review; and promulgate guidance on the development of abuse-deterrent drug products (§1122).
- Requires the Secretary to work with other regulatory authorities, medical research companies, and international organizations to harmonize global clinical trial standards for medical products, in order to (1) enhance medical product development; (2) facilitate the use of foreign data; and (3) reduce duplicative studies; and includes savings clause that this provision would not alter the current standards for premarket review of medical products (§1123).
- Requires the Secretary, in deciding whether to approve, license, or clear a drug or device, to accept data from clinical trials outside the United States, as long as such data meet applicable standards; and requires the Secretary to provide a sponsor with a written explanation in the event that such data were found to be inadequate (§1123).
- Requires the Secretary, within one year of enactment, to establish a strategy and implementation plan, consistent with user fee program performance goals, for advancing regulatory science for medical products, and to identify in such plan a vision and priorities related to medical product decision-making, and ways to address regulatory and scientific gaps, among other stated requirements; and requires the Secretary to include a report on progress on those goals as part of the FY2014 and FY2016 performance reports required for the prescription drug, medical device, generic drug, and biosimilar biological product user fee programs (§1124).
- Requires the Secretary to report, not later than one year after enactment, to Congress on the development and implementation of a plan to modernize FDA's information technology systems and align them with the strategic goals of the agency, consistent with existing GAO recommendations; additionally, requires GAO to report, by January 1, 2016, on the FDA's progress to meet the goals set out in such plan (§1125).
- Requires the Secretary to intensify and expand activities to enhance scientific knowledge regarding nanomaterials included or intended for inclusion in FDA-regulated products to address potential toxicology, potential benefit of new therapies, and the effects on and interactions with biological systems (§1126).
- Requires GAO, within one year of enactment, to report, as specified, on problems posed by online pharmacy websites that violate state or federal law (§1127).
- Requires a report from the FDA Commissioner to Congress within one year of enactment with details regarding FDA interactions with small businesses, including outreach, grants, and barriers encountered (§1128).
- Prohibits any restriction on lawful communication by a U.S. Public Health Service Commissioned Officer with a Member of Congress or the HHS Inspector

General, providing a so-called "whistleblower" protection comparable to such protections among the armed services (§1129).

- Sets dates for product compliance with final rule for labeling and effectiveness of sunscreen products for over-the-counter human use (§1130).
- Requires the Secretary to submit to Congress within one year of enactment an integrated management plan to improve the efficiency and effectiveness of the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiological Health, including workforce performance measures (§1131).
- Amends the requirements and procedures, including timing of review by the Secretary, concerning assessments of approved risk evaluation and mitigation strategies (REMS)[50] and their modification; and requires the Secretary to issue guidance on types of modifications (§1132).
- Temporarily extends the period during which a manufacturer can obtain tentative approval of a generic drug application before forfeiting the marketing exclusivity for being the first generic version (§1133).
- Adds a 270-day deadline by which, in response to a petition, the Secretary must issue a final substantive determination on whether a drug withdrawal was due to its safety and effectiveness (§1134).
- Shortens from 180 days to 150 days the deadline by which the Secretary must take final agency action on a petition regarding a new drug application that refers to data submitted to FDA from another approved product or an abbreviated new drug application; and adds a biosimilar biologics license application to that requirement (§1135).
- Requires, beginning not before two years after final guidance is issued, applications for drugs and biologics to be submitted in electronic format; and requires, beginning after final guidance is issued, pre-submissions, submissions, and supplemental information for medical devices to include an electronic copy of such materials (§1136).
- Requires the Secretary to develop and implement strategies to solicit patients' views during regulatory discussions, including permitting the participation of a patient representative in agency meetings with medical product sponsors (§1137).
- Requires, within one year of enactment, the Commissioner to review, modify, and make publicly available the FDA communication plan to inform health care providers and patients of the benefits and risks of medical products, with special focus on underrepresented subpopulations, including racial subgroups (§1138).
- Requires the Secretary to hold a public meeting and solicit stakeholder input regarding scheduling of products containing hydrocodone under the Controlled Substances Act (§1139).

[50] FDAAA (P.L. 110-85) authorized the Secretary to require a risk evaluation and mitigation strategy in connection with the approval of a new drug application or at other times if it "is necessary to ensure that the benefits of the drug outweigh the risks of the drug." A REMS may include required patient or healthcare provider information and elements to assure safe use (ETASU) such as a restriction on distribution or use.

- Requires a report by GAO within one year of enactment on the benefits and efficiencies of electronic patient labeling of prescription drugs as a substitute or partial substitute for paper labeling (§1140).
- Authorizes the Secretary, in consultation with the Attorney General, to "facilitate … the development of recommendations on interoperability standards" for the interstate exchange of prescription drug monitoring program (PDMP) information by states receiving specified federal grants; requires the Secretary, "in facilitating the development of recommendations," to consider specified topics; and requires the Secretary to submit a report on enhancing PDMP interoperability, to include specified contents (§1141).
- Regarding advisory committee member conflicts of interest, strikes the provision limiting the number of exceptions (such as waivers under the provisions of the criminal financial conflict-of-interest statute [18 U.S.C. 208]) the Secretary could grant (as authorized for FY2008 through FY2012) and maintains the content and timing requirements for public disclosure of committee member financial interests that the Secretary (according to 18 U.S.C. 208), adding as a reason for an exception that there is a public health interest in having the expertise available to the committee (§1142).
- Requires the Secretary to develop and implement outreach strategies for potential members of advisory committees to ensure the most current expert advice; modifies the required content of the required annual report from the Secretary on advisory committee conflicts of interest; requires the Secretary to review and update, as necessary, guidance with respect to advisory committees regarding disclosure of conflicts of interest; and requires the Secretary to issue guidance that describes the FDA process for reviewing financial conflicts of interest reported by advisory committee members that do not meet the definition of disqualifying interest (§1142).
- Prohibits, for five years, the FDA from issuing draft or final guidance on the regulation of laboratory-developed tests (LDTs) prior to notifying the House Energy and Commerce Committee and the Senate Committee on Health, Education, Labor, and Pensions of both their intent to do so, and the details of such intended action (§1143).

Subtitle D—Synthetic Drugs

In general, Subtitle D—Synthetic Drugs, the Synthetic Drug Abuse Prevention Act of 2012:

- Adds specified synthetic drugs, including those that mimic the effects of cannabis marijuana, to schedule I (the most restrictive schedule, for drugs with high risk of abuse for which there are no recognized medical uses) under the Controlled Substances Act (CSA); also, with regard to temporary scheduling, extends the initial period of temporary scheduling from one year to two years and the extension of temporary scheduling from 6 months to one year (§§1151-1153).

Appendix A. Time-Specific Requirements of Federal Entities in FDASIA[51]

Throughout FDASIA, Congress has directed certain actions to be done by specified entities within specified time periods. It directs most of the federal actions to the Secretary, Department of Health and Human Services (HHS, the Secretary); several actions are required of other federal entities. FDASIA also requires many actions of the regulated industry.

This appendix lists the *time-specific requirements* (meaning actions required to be completed within a specific time period) of *federal entities*[52] in FDASIA (see methodology section below).[53] These tables present the requirements as contained in FDASIA; CRS will not update this report to track agency progress toward meeting or completing these requirements. The HHS Secretary is responsible for more than 90% of the requirements, and FDA is maintaining a website to reflect the agency's tracking of those activities.[54]

Methodology

This section explains how requirements were selected for inclusion in the appendix and how dates are presented in the tables.

Selection criteria. This appendix includes provisions that require action by the responsible entity (the actor) (1) by a specific date (e.g., not later than January 15, 2014); (2) within a specified number of days or months of a specified event (e.g., not later than 60 days before the start of the fiscal year); or (3) with a timed aspect not pegged to a date or event (e.g., at least every five years). Requirements are not included if (1) the timing is conditionally defined (e.g., if a sponsor submits a request, the Secretary must respond not later than 60 days from the submission), or (2) no explicit time is noted (e.g., the Secretary must maintain an up-to-date list of drugs in shortage). For linked requirements (e.g., draft guidance and final guidance), the entire set of requirements is included if at least one requirement meets the selection criteria.

[51] The material in this appendix was originally presented as a Congressional Distribution Memorandum entitled "Time-specific requirements of federal entities in the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144," by Susan Thaul, dated December 6, 2012.

[52] The statutorily designated actor is almost always the Secretary of Health and Human Services. When FDASIA added a specification, such as "the Secretary, acting through the Commissioner of Food and Drugs," that detail is noted. Most of the actions required of the Secretary are likely to be carried out by FDA staff under the Commissioner of Food and Drugs. FDASIA also requires four actions of the Comptroller General of the Government Accountability Office, and one each of the Commissioner of Food and Drugs, the Attorney General, and the Architectural and Transportation Barriers Compliance Board. This appendix does not include requirements placed on regulated industries or any other non-federal entity.

[53] Congress set the requirements and associated deadlines in FDASIA in July 2012 before any FY2013 appropriations bill was passed. The continuing appropriations resolution enacted just before the start of FY2013 authorized FY2012 user fee rates for October 1, 2012 through March 27, 2013 (H.J.Res. 117, Continuing Appropriations Resolution, 2013, enacted as P.L. 112-175 on September 28, 2012). Therefore, the funding available to FDA for at least the first six months of the fiscal year will not include, for example, the increased revenue from the prescription drug and medical device user fee programs that FDASIA authorized.

[54] FDA, "FDASIA-TRACK," http://www.fda.gov/AboutFDA/Transparency/track/ucm328907.htm.

Presentation of dates. The legislative language in FDASIA differs across titles and sections in how it refers to the timing of required actions. To achieve consistent presentation of timing, this appendix presents (with very few exceptions) time-specific requirements in date form. When FDASIA provides an actual date, the appendix uses that date. When FDASIA refers to an event, the date is calculated; for example, when the legislative language reads "not less than 60 days before the start of the fiscal year," the appendix presents this as August 2, the calculated number of days from October 1. When a time-specific requirement is not pegged to a date or event (e.g., at least every five years), it is noted as such. When a requirement recurs annually, the table shows only the month and day that action must occur each year.

For efficiency of presentation and overall view of timed requirements, when a time-specific requirement is defined by a range, the table lists the last day of the range. For example, tables in this appendix would list the timing reference as "July 9, 2013," in each of the following three situations:

As Presented in FDASIA	As Presented in Appendix
On July 9, 2013	July 9, 2013
Not later than July 9, 2013	July 9, 2013
Not later than one year after enactment	July 9, 2013

Comparison to FDA Implementation Tracking Chart

On November 27, 2012, FDA created a website[55] that lists the "requirements with specific statutory dates set by Congress"; the agency intends to update the chart to "communicate its progress." Comparing the information that FDA posted with the material in this appendix reveals some differences in scope and level of detail.[56] The main differences are as follows:

- The FDA chart includes only deliverables for which FDA is responsible. This appendix includes actions required of all federal entities.
- The FDA chart includes actions specified in the letters from the Secretary to Congress that present the performance goals negotiated with industry for the user fee programs.[57] This appendix includes only requirements specified in FDASIA.
- The FDA chart includes a column that FDA will use to publicly track its progress as it completes each requirement. This appendix does not duplicate that effort.

[55] FDA, "FDASIA-TRACK," http://www.fda.gov/AboutFDA/Transparency/track/ucm328907.htm.

[56] The FDA website does not include methodology notes. For consistency, all dates in this appendix that were converted from textual phrases (such as "not later than 120 days after enactment") using an on-line date calculator: "Days from Date Calculator," http://www.convertunits.com/dates/daysfromdate/. For several sets of provisions, the FDA chart and this appendix show them grouped either together or separately. At times, the dates in the FDA chart and this appendix differ by one or two days; CRS has not evaluated FDA's methodology and cannot comment on how FDA calculated or chose the dates.

[57] For background on the use of negotiated performance goals and their relationship to the user fee provisions in the FFDCA, see these CRS reports: CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): Issues for Reauthorization (PDUFA V) in 2012*, by Susan Thaul; CRS Report R42508, *The FDA Medical Device User Fee Program*, by Judith A. Johnson; and CRS Report R42540, *Proposed FDA User Fee Acts: Generic Drug User Fee Amendments of 2012 (GDUFA) and Biosimilar User Fee Act of 2012 (BSUFA)*, by Susan Thaul and Judith A. Johnson.

Legal Effect of Deadlines[58]

As a matter of administrative law, the enforceability of statutory deadlines is determined primarily via private civil litigation against the agency for failure to comply with the deadline. Although a court may compel an agency to take action when the agency has "unreasonably delayed," courts generally provide agencies deference in order to avoid dictating how an agency should allocate its limited resources. In Telecommunications Research & Action Center v. FCC (TRAC), the Circuit Court of Appeals for the District of Columbia (D.C. Circuit) established a set of factors to consider when determining whether an agency has delayed unreasonably in taking a required action. In TRAC, the D.C. Circuit noted that courts should be guided by a "rule of reason" when determining whether the agency has unreasonably delayed, but also stated that "where Congress has provided a timetable or other indication of the speed with which it expects the agency to proceed in the enabling statute, that statutory scheme may supply content for this rule of reason."

The D.C. Circuit's language in TRAC provides that a court should consider congressionally imposed deadlines, but also indicates that a court should not necessarily find that an agency delayed unreasonably based solely on the fact that the agency missed a statutory deadline. In one prominent example, the D.C. Circuit declined to compel a rulemaking by the Mine Safety and Health Administration (MSHA) even though the agency had violated a statutory deadline for completing the regulation. The court agreed, however, to retain jurisdiction and required MSHA to report regularly on the status of its rulemaking process. In an administrative adjudication context, the D.C. Circuit similarly refused to compel the Food and Drug Administration (FDA) to complete the review of a generic drug application even though the FDA missed a statutory deadline by a significant margin. Therefore, although the FDASIA imposes statutory deadlines on various executive agencies, the enforceability of these statutory deadlines in court would be determined through civil litigation on a case-by-case basis. In lieu of relying on civil litigation to enforce statutory deadlines, Congress may also use their political powers, such as congressional oversight hearings and/or other forms of legislative pressure, to compel agencies to comply with mandated deadlines.

Tables

Tables 1 through 11 correspond to Titles I through XI of FDASIA.[59] Rows are ordered by FDASIA section, listed in the first column. Other columns provide the relevant section, if any, in the Federal Food, Drug, and Cosmetic Act (FFDCA), the Public Health Service Act (PHSA), the Controlled Substances Act (CSA), or the Americans with Disabilities Act (ADA), and its U.S. Code citation;[60] the actor; the required action; and the timing reference. A list of abbreviations and acronyms appears as **Appendix B**.

[58] Daniel T. Shedd, Legislative Attorney, American Law Division, provided the material on the legal effect of deadlines.

[59] The body of this report provides descriptions of the provisions in FDASIA, including those without time-specific federal agency requirements.

[60] These laws are in the U.S. Code as follows: Federal Food, Drug, and Cosmetic Act—21 U.S.C. 301 et seq., Public Health Service Act—42 U.S.C. 201 et seq., Controlled Substances Act—21 U.S.C. 801 et seq., and Americans with Disabilities Act—42 U.S.C. 12101 et seq.

Table A-1. Federal Agency Timed Requirements in FDASIA Title I—Fees Relating to Drugs

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
103	FFDCA 736(c) 21 USC 379h	Secretary	Set and publish inflation adjustment for drug user fees annually. Set and publish workload adjustment for drug user fees annually. Establish application, product, and establishment fees annually.	Not specified Not specified August 2[a]
103	FFDCA 736(c) 21 USC 379h	Secretary	Contract with independent firm to review adjustment and publish first and second reviews for public comment.	First review: September 30, 2013 Second review: September 30, 2015
104	FFDCA 736B(a) 21 USC 379h-2	Secretary	Submit annual performance report to Congress. [b]	January 28[a]
104	FFDCA 736B(b) 21 USC 379h-2	Secretary	Submit annual fiscal report to Congress.	January 28[a]
104	FFDCA 736B(d) 21 USC 379h-2	Secretary	Transmit to Congress recommendations regarding goals and plans for meeting the goals for the next 5-year reauthorization of PDUFA. In preparation of the recommendations, (1) consult with the congressional authorizing committees, scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry; (2) announce and hold a public meeting, obtain written public comments, and publish comments; (3) hold periodic consultation with representatives of patient and consumer advocacy groups during negotiations with the regulated industry; (4) make publicly available minutes of all negotiation meetings between FDA and the regulated industry; and (5) publish recommendations (to Congress and FDA website), allow comment, hold public meeting, revise recommendations as necessary.	January 15, 2017

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. PDUFA = Prescription Drug User Fee Amendments. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

a. Dates shown with no year repeat annually.

b. FDASIA Sec. 1124 adds content requirements for the FY2014 and FY2016 reports.

Table A-2. Federal Agency Timed Requirements in FDASIA Title II—Fees Relating to Devices

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
203	FFDCA 738(c) 21 USC 379j	Secretary	Establish fees annually, after setting and publishing the inflation adjustment for device user fees and the volume-based adjustment to establishment registration.	August 2 [a]
204	FFDCA 738A(b) 21 USC 379j-1	Secretary	Transmit to Congress recommendations regarding goals and plans for meeting the goals for the next 5-year reauthorization of MDUFA. In preparation of the recommendations, (1) consult with the congressional authorizing committees, scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry; (2) announce and hold a public meeting, obtain written public comments, and publish comments; (3) hold periodic consultation with representatives of patient and consumer advocacy groups during negotiations with the regulated industry; (4) make publicly available minutes of all negotiation meetings between FDA and the regulated industry; and (5) publish recommendations (to Congress and FDA website), allow comment, hold public meeting, revise recommendations as necessary.	January 15, 2017
204	FFDCA 738A(a) 21 USC 379j-1	Secretary	Submit annual performance report to Congress. [b]	Not specified [c]
204	FFDCA 738A(a) 21 USC 379j-1	Secretary	Submit annual fiscal report to Congress.	January 28 [a]
204	FFDCA 738A(a) 21 USC 379j-1	Secretary	Make publicly available quarterly and annual information reported to industry pursuant to letters of agreement.	March 1, May 30, August 29, and November 29; [a] or January 28 [a]

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. MDUFA = Medical Device User Fee Amendments. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

a. Dates shown with no year repeat annually.

b. FDASIA Sec. 1124 adds content requirements for the FY2014 and FY2016 reports.

c. FDASIA replaced the language in FFDCA 738A(a), which had required the Secretary to submit the report not later than 120 days after the end of the fiscal year (which is January 28). The FDASIA language, however, did not include the timing reference. All other annual performance and fiscal reports that FDASIA requires for PDUFA, GDUFA, and BSUFA have the January 28 deadline.

Table A-3. Federal Agency Timed Requirements in FDASIA Title III—Fees Relating to Generic Drugs

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
302	FFDCA 744B(a)(1)&(d)(1) 21 USC 379j-42	Secretary	Establish and publish the one-time backlog fee for an abbreviated new drug application pending on October 1, 2012.	October 31, 2012
302	FFDCA 744B(a)(2)&(d)(1) 21 USC 379j-42	Secretary	Establish and publish the drug master file (DMF) fee for FY2013.	October 31, 2012
302	FFDCA 744B(a)(2)&(d)(2) 21 USC 379j-42	Secretary	Establish and publish the DMF fees for each of FY2014 through FY2017.	August 2 [a,b]
302	FFDCA 744B(a)(3)&(d)(1) 21 USC 379j-42	Secretary	Establish and publish the abbreviated new drug application (ANDA) and prior approval supplement (PAS) fees for FY2013.	October 31, 2012
302	FFDCA 744B(a)(3)&(d)(2) 21 USC 379j-42	Secretary	Establish and publish the ANDA and PAS fees for each of FY2014 through FY2017.	August 2 [a,b]
302	FFDCA 744B(a)(4)&(d)(1) 21 USC 379j-42	Secretary	Establish and publish the generic drug facility fee and the active pharmaceutical ingredient (API) facility fee for FY2013.	January 14, 2013
302	FFDCA 744B(a)(4)&(d)(2) 21 USC 379j-42	Secretary	Establish and publish the generic drug and API facility fees for each of FY2014 through FY2017.	August 2 [a,b]
302	FFDCA 744B(d)(3) 21 USC 379j-42	Secretary	Determine fee for API information not included by reference to an API DMF according to provided formula.	For FY2013: October 31, 2012 For each of FY2014 through FY2017: August 2 [a]
302	FFDCA 744B(f) 21 USC 379j-42	Secretary	Publish notice requiring facility (as defined) owners to submit required information to identify facilities.	October 1, 2012
303	FFDCA 744C(a) 21 USC 379j-43	Secretary	Submit annual performance report to Congress.	January 28 [a]
303	FFDCA 744C(b,c) 21 USC 379j-43	Secretary	Submit annual fiscal report to Congress.	January 28 [a]

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
303	FFDCA 744C(d) 21 USC 379j-43	Secretary	Transmit to Congress recommendations regarding goals and plans for meeting the goals for the next 5-year reauthorization of GDUFA. In preparation of the recommendations, (1) consult with the congressional authorizing committees, scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the generic drug industry; (2) announce and hold a public meeting, obtain written public comments, and publish comments; (3) hold periodic consultation with representatives of patient and consumer advocacy groups during negotiations with the generic drug industry; (4) make publicly available minutes of all negotiation meetings between FDA and the generic drug industry; and (5) publish recommendations (to Congress and FDA website), allow comment, hold public meeting, revise recommendations as necessary.	January 15, 2017
308	FFDCA 715 21 USC 379d-4	Secretary	Prepare and submit annual report to Congress with the number of applications that met goals, the average total time to decision, the total number of applications that were pending for more than 10 months on the date of enactment, and the number of those pending applications on which FDA took final regulatory action in the previous FY.	January 28 [a]

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. FY = fiscal year. GDUFA = Generic Drug User Fee Amendments. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

a. Dates shown with no year repeat annually.

b. FFDCA Sec. 744B refers to fee setting in paragraphs (a) Types of Fees and (d) Annual Fee Setting. In (a)(2)(C)(ii), the Secretary is directed to publish a notice announcing the DMF fee "Not later than 60 days before the start of each of fiscal years 2014 through 2017." The same timing language is used in (a)(3)(B)(ii) for ANDA and PAS fees. However, (a)(4)(C)(ii), regarding generic drug and API facility fees, directs the timing of the notice to be "Within the timeframe specified in subsection (d)(2)." FFDCA 744B(d)(2) directs the Secretary to establish the DMF, ANDA, PAS, generic drug facility, and API facility fees "Not more than 60 days before the first day of each of fiscal years 2014 through 2017." The directions in paragraph (a) point to notice not later than August 2, and the directions in paragraph (d) point to notice not before August 2. The paragraph (d) language may be a drafting error. If it is not, FFDCA Sec. 744B appears to contain contradictory requirements.

Table A-4. Federal Agency Timed Requirements in FDASIA Title IV—Fees Relating to Biosimilar Biological Products

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
402	FFDCA 744H(b)(1) 21 USC 379j-52	Secretary	Establish the amount of each fee for a biosimilar biological product (initial development fee, annual development fee, reactivation fee, application fee, establishment fee, and product fee) using provided formulas based on the inflation-adjusted PDUFA application fee.	August 2 [a]
403	FFDCA 744I(a,c) 21 USC 379j-53	Secretary	Submit annual performance report to Congress.	January 28 [a]
403	FFDCA 744I(b,c) 21 USC 379j-53	Secretary	Submit annual fiscal report to Congress.	January 28 [a]
403	FFDCA 744I(d) 21 USC 379j-53	Secretary	Contract with independent firm to study workload volume and full costs and publish interim and final results.	Interim: June 1, 2015 Final: September 30, 2016
403	FFDCA 744I(e) 21 USC 379j-53	Secretary	Transmit to Congress recommendations regarding goals and plans for meeting the goals for the next 5-year reauthorization of BSUFA. In preparation of the recommendations, (1) consult with the congressional authorizing committees, scientific and academic experts, health care professionals, representatives of patient and consumer advocacy groups, and the regulated industry; and (2) publish recommendations (to Congress and FDA website), allow comment, hold public meeting, revise recommendations as necessary.	January 15, 2017
408	FFDCA 715 21 USC 379d-4	Secretary	Prepare and submit report to Congress with the number of applications for approval filed under PHSA Sec. 351(k), and the percentage of those that the Secretary approved. Include in annual performance report an explanation of how FDA is managing the biological product review program to ensure that the user fees collected under part 2 are not used to review an application under PHSA Sec. 351(k).	January 28 [a]

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: BSUFA = Biosimilar User Fee Act. FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. PDUFA = Prescription Drug User Fee Amendments. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

a. Dates shown with no year repeat annually.

Table A-5. Federal Agency Timed Requirements in FDASIA Title V—Pediatric Drugs and Devices

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
503	21 USC 355a note	Secretary	Issue internal standard operating procedures for the internal Pediatric Review Committee's review of specified study plans and written requests under BPCA and PREA.	July 9, 2013
504	21 USC 355a note	Secretary	Make available the medical, statistical, and clinical pharmacology reviews of (and agency requests for) studies submitted between January 4, 2002, and September 27, 2007, under BPCA that resulted in six months of market exclusivity and a labeling change.	July 9, 2015
506	FFDCA 505B(e) 21 USC 355c	Secretary	Promulgate proposed regulations and issue guidance to implement pediatric study plan requirements.	July 9, 2013
508	21 USC 355c-1	Secretary	Prepare and submit reports, with specified content and to include stakeholder input, to Congress and the public on the implementation of BPCA and PREA.	Solicit feedback: January 11, 2016[a] and every 5 years thereafter Report: July 9, 2016 and every 5 years thereafter
510	—	Secretary	Hold a public meeting to discuss ways to encourage and accelerate the development of new therapies for pediatric rare diseases. Report on a strategic plan on accelerated development of new therapies for pediatric rare diseases.	January 9, 2014 NLT 180 days after public meeting

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: BPCA = Best Pharmaceuticals for Children Act. FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. NLT = not later than. PREA = Pediatric Research Equity Act. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

a. Stated as "at least 180 days prior to the submission of each report ... "

Table A-6. Federal Agency Timed Requirements in FDASIA Title VI—Medical Device Regulatory Improvements

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
604	FFDCA 510(n) 21 USC 360	Secretary	Submit report to Congress "regarding when a premarket notification under subsection (k) should be submitted for a modification or change to a legally marketed device."	January 9, 2014
608	FFDCA 515(i) 21 USC 360e	Secretary	Issue an administrative order (after publishing proposed order in the FR, a meeting of a device classification panel, and consideration of comments) regarding devices that were "introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, and which are subject to revision of classification under paragraph (2) ..."	July 9, 2014
611	FFDCA 523(b) 21 USC 360m	Secretary	Establish and publish criteria to reaccredit or deny reaccreditation of persons who review "reports submitted under section 360(k) [FFDCA 510(k)] ... " and make recommendations "regarding the initial classification of devices under section 360c(f)(1) [FFDCA 513(f)(1)]."	November 6, 2012
614	FFDCA 519(f) 21 USC 360i	Secretary	Issue and implement regulations to establish "a unique device identification system ... requiring the label of devices to bear a unique identifier ... taking into account patient access to medical devices and therapies."	Proposed regulations: December 31, 2012 Finalize regulations: NLT 6 months after close of comment period Implement final regulations "with respect to devices that are implantable, life-saving, and life sustaining" NLT 2 years after final regulations
617	FFDCA 520(b) 21 USC 360j	Secretary	Issue final guidance on the replication of multiple custom devices.	July 9, 2014
618	—	Secretary, through the Commis-sioner of Food and Drugs	Post a report with "a proposed strategy and recommendations on an appropriate, risk-based regulatory framework pertaining to health information technology, including mobile medical applications ..."	January 9, 2014

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
620	21 USC 360e-1 note	Secretary	Issue rule implementing FFDCA 515A(a)(2), which requires a pediatric device applicant for a humanitarian use exemption or premarket approval to 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."	Proposed rule: December 31, 2012 Final rule: December 31, 2013

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. NLT= Not Later Than. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

Table A-7. Federal Agency Timed Requirements in FDASIA Title VII—Drug Supply Chain

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
704	FFDCA 510(p) 21 USC 360	Secretary	Maintain an electronic database of domestic and foreign drug establishment registrations and listings.	NLT 2 years after Secretary specifies a unique facility identifier (UFI)
705	FFDCA 510(h) 21 USC 360	Secretary	Report annually on inspections of establishments.	February 1, 2014 and annually thereafter
707	FFDCA 501 21 USC 351 note	Secretary	Issue guidance on what would constitute delaying, denying, or limiting inspection, or refusing to permit entry or inspection.	July 9, 2013
708	FFDCA 801(a) 21 USC 381	Secretary	Issue regulations regarding notice and opportunity to appear before the Secretary regarding destruction of adulterated, misbranded, or counterfeit drugs offered for import.	Final regulations: July 9, 2014
709	21 USC 334 note	Secretary	Promulgate and implement regulations regarding administrative detention authority with respect to drugs.	July 9, 2014
713	FFDCA 801(r) 21 USC 381	Secretary	Adopt final regulations implementing information requirements the Secretary may set regarding the regulatory status of a drug imported or offered for import, and related facility information such as indication of compliance with current good manufacturing practice.	January 9, 2014

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
714	21 USC 381 note	Secretary	Promulgate, in consultation with the Secretary of Homeland Security acting through U.S. Customs and Border Protection, regulations required to carry out FFDCA Sec. 801(s) (required registration of commercial importers and establishment of good importer practices).	July 9, 2015

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. NLT = not later than. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

Table A-8. Federal Agency Timed Requirements in FDASIA Title VIII—Generating Antibiotic Incentives Now

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
801	FFDCA 505E 21 USC 355f	Secretary	Adopt final regulations (to include a list of qualifying pathogens) implementing FFDCA Sec. 505E (Extension of Exclusivity for New Qualified Infectious Disease Products). Review, modify and publish list.	July 9, 2014 Every 5 years, or more often as needed
805	—	Secretary	Report to Congress (in consultation with FDA, CDC, and other appropriate agencies) to reassess qualified infectious disease product incentives.	July 9, 2017
806	21 USC 355 note	Secretary	Publish guidance on pathogen-focused antibacterial drug development.	Draft guidance: June 30, 2013 Final guidance: December 31, 2014

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: CDC = Centers for Disease Control and Prevention. FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

Table A-9. Federal Agency Timed Requirements in FDASIA Title IX—Drug Approval and Patient Access

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
901	21 USC 356 note	Secretary	Issue guidance to implement the amendments to FFDCA Sec. 506 regarding fast track products and the accelerated approval process.	Draft guidance: July 9, 2013 Final guidance: NLT 1 year after issuance of draft guidance and opportunity for public comment
902	21 USC 356 note	Secretary	Issue guidance implementing requirements with respect to breakthrough therapies.	Draft guidance: January 9, 2014 Final guidance: NLT 1 year after close of comment period for the draft guidance
904	29 USC 792 note (Rehabilitation Act of 1973 as amended)	Architectural and Transportation Barriers Compliance Board (an independent federal agency dealing with accessible design)	Board: Convene a stakeholder working group to develop best practices on access to information on prescription drug container labels for individuals who are blind or visually impaired. Working group: Develop best practices for pharmacies to ensure that blind and visually impaired individuals have safe, consistent, reliable, and independent access to the information on prescription drug container labels.	Not specified Best practices: July 9, 2013
		Comptroller General	Review and report on the extent to which pharmacies are using best practices regarding accessible drug container labels.	Review: beginning 18 months after completion of the development of best practices regarding accessible drug container labels Report: September 30, 2016
907	—	Secretary, acting through the Commissioner of Food and Drugs	Publish a report (with specified contents) pertaining to protection of sponsors' confidential commercial information, addressing the extent to which clinical trial participation and the inclusion of safety and effectiveness data by demographic subgroups is included in applications to FDA. Publish action plan (on FDA website and provide to Congress) with recommendations, as appropriate, on demographic subgroup data quality and use.	July 9, 2013 Not later than one year after publication of the report

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
908	FFDCA 529(c) 21 USC 360ff	Secretary	Establish a user fee program for sponsor of drug application under a priority review voucher. Determine, annually, amount of the priority review user fee based on specified formula.	Not specified September 30, 2013 and annually thereafter

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. NLT = not later than. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

Table A-10. Federal Agency Timed Requirements in FDASIA Title X—Drug Shortages

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
1001	FFDCA 506C(i) 21 USC 356c	Secretary	Adopt final regulation implementing this section.	January 9, 2014
1002	FFDCA 506C-1 21 USC 356c-1	Secretary	Submit annual report to Congress on drug shortages, with specified content.	December 31, 2013 and annually thereafter
1003	FFDCA 506D 21 USC 356d	Secretary	"Establish a task force to develop and implement a strategic plan for enhancing the Secretary's response to preventing and mitigating drug shortages." Publish the strategic plan and submit it to Congress.	Task force: Not specified Plan: July 9, 2013
1006	21 USC 826a (within the CSA)	Attorney General	Submit annual report to Congress on drug shortages with specified content.	January 9, 2013 and annually thereafter
1008	—	Comp-troller General	Conduct study and submit report to Congress, considering specified questions and in consultation with specified stakeholders, "to examine the cause of drug shortages and formulate recommendations on how to prevent or alleviate such shortages."	January 9, 2014

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

Table A-11. Federal Agency Timed Requirements in FDASIA Title XI—Other Provisions

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
1112	21 USC 360ddd note	Secretary	After obtaining input from medical gas manufacturers and members of the public, submit report to Congress regarding whether changes to federal regulations are necessary regarding medical gases.	January 9, 2014
1121	21 USC 379d-5	Secretary	Issue guidance describing FDA policy on the promotion of FDA-regulated products using the Internet, including social media.	July 9, 2014
1122	—	Secretary	After reviewing current federal initiatives and identifying gaps and opportunities with respect to ensuring: (1) the safe use of prescription drugs with potential for abuse and (2) the treatment of prescription drug dependence, issue a report on findings of the review (to be posted on the HHS website).	July 9, 2013
1122	21 USC 355 note	Secretary	Promulgate guidance on the development of abuse-deterrent drug products.	January 9, 2013
1124	21 USC 393 note	Secretary	Develop a strategy and implementation plan, according to specified requirements, for advancing regulatory science for medical products to promote public health and advance innovation in regulatory decisionmaking; make strategy and plan consistent with performance goals specified in letters to the Congress regarding the prescription drug (PDUFA) and medical device (MDUFA) user fee agreements for FY2013 through FY2017.	July 9, 2013
1124	21 USC 393 note	Secretary	Include in specified performance reports to Congress required for PDUFA and MDUFA a report on progress, as specified, made with respect to advancing specified regulatory science priorities and integrating the advances.	January 28, 2015 and January 28, 2017 [a]

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
1125	21 USC 393 note	Secretary	Report to Congress on "the milestones and a completion date for developing and implementing a comprehensive information technology strategic plan" and other specified content regarding information technology; and "develop a documented enterprise architecture program management plan," "a skills inventory, needs assessment, gap analysis, and initiatives to address skills gaps as part of a strategic approach to information technology human capital planning."	July 9, 2013
1125	21 USC 393 note	Comp-troller General	Issue a report regarding the comprehensive information technology strategic plan and FDA progress on specified actions.	January 1, 2016
1127	—	Comp-troller General	Submit report to Congress that "describes any problems [including those specified] posed by pharmacy Internet Web sites that violate Federal or State law."	July 9, 2013
1128	—	Commis-sioner of Food and Drugs	Submit report on specified aspects of agency activities regarding small businesses.	July 9, 2013
1131	—	Secretary	Submit to Congress a strategic integrated management plan, with specified content, for the FDA Centers for Drug Evaluation and Research, Biologics Evaluation and Research, and Devices and Radiological Health.	July 9, 2013
1132	21 USC 355-1	Secretary	Issue guidance that describes the types of modifications to approved risk evaluation and mitigation strategies to be considered minor modifications.	July 9, 2013
1138	21 USC 399f	Secretary, acting through the Commis-sioner of Food and Drugs	Review and modify, as necessary, the FDA's communication plan and publicly post a report "to inform and educate health care providers and patients on the benefits and risks of medical products, with particular focus on underrepresented subpopulations, including racial subgroups."	July 9, 2013
1139	—	Secretary	Hold a public meeting and solicit stakeholder input regarding scheduling of products containing hydrocodone under the Controlled Substances Act and post transcript of meeting on FDA website.	September 7, 2012, if practicable

FDASIA Section	Current Law Citation	Actor	Required Action	Timing Reference
1141	—	Secretary	Submit a report to Congress on "enhancing the interoperability of State prescription drug monitoring programs and other technologies and databases used for detecting and reducing fraud, diversion, and abuse of prescription drugs."	July 9, 2012
1142	FFDCA 712(e) 21 USC 379d-1	Secretary	Submit annual report to Congress with specified information about advisory committee member recruitment, attendance, and conflict disclosures.	Report: February 1 [b] Public availability: NLT 30 days after report submission
1142	FFDCA 712(f) 21 USC 379d-1	Secretary	Review, and update if necessary, the FDA guidance regarding disclosure of conflicts of interest regarding advisory committees.	Not less than once every 5 years

Source: CRS analysis of P.L. 112-144, the Food and Drug Administration Safety and Innovation Act (FDASIA).

Notes: FDA = Food and Drug Administration. FFDCA = Federal Food, Drug, and Cosmetic Act. MDUFA = Medical Device User Fee Amendments. NLT = Not Later Than. PDUFA = Prescription Drug User Fee Amendments. Secretary = Secretary of the Department of Health and Human Services. USC = U.S. Code.

a. FDASIA Sec. 1124 adds required content to the FY2014 and FY2015 performance reports required by PDUFA and MDUFA (FFDCA Secs. 736B(a) and 738A(a). Those reports are due not later than 120 days after the end of the fiscal year, which is January 28.

b. Dates shown with no year repeat annually.

Appendix B. Abbreviations and Acronyms

ADA	Americans with Disabilities Act
ANDA	abbreviated new drug application
API	active pharmaceutical ingredient
BPCA	Best Pharmaceuticals for Children Act
BSUFA	Biosimilar User Fee Act of 2012
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CSA	Controlled Substances Act
CY	calendar year
DMF	drug master file
FDA	Food and Drug Administration
FDASIA	Food and Drug Administration Safety and Innovation Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FR	*Federal Register*
FY	fiscal year
GAO	Government Accountability Office
GD	generic drug
GDUFA	Generic Drug User Fee Amendments of 2012
HHS	Department of Health and Human Services
MDUFA	Medical Device User Fee Amendments of 2012
NLT	not later than
NMT	not more than
PAS	prior approval supplement
PDUFA	Prescription Drug User Fee Amendments of 2012
PHSA	Public Health Service Act
PREA	Pediatric Research Equity Act
REMS	risk evaluation and mitigation strategy
Secretary	Secretary of HHS
USC	U.S. Code

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