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FDA Reauthorization Act of 2017 (FDARA, P.L. 115-52)

Updated September 21, 2017

Congressional Research Service
https://crsreports.congress.gov
R44961

CRS REPORT
Prepared for Members and
Committees of Congress

Summary

Food and Drug Administration (FDA) review of medical products (human drugs and devices) is funded through a combination of annual discretionary appropriations from Congress (budget authority) and user fees collected from industry. The human medical product user fee programs require reauthorization every five years to continue uninterrupted. Prior to the passage of the Food and Drug Administration Reauthorization Act of 2017 (FDARA, P.L. 115-52), these programs were set to expire on September 30, 2017. The reauthorization legislation typically includes additional provisions related to FDA, since for many the bill is considered "must-pass" legislation in order to not interrupt FDA product review activities.

FDARA continues the five-year reauthorization cycle of the human medical product user fee programs; this reauthorization allows FDA to keep collecting user fees and using the revenue to support, among other things, the review of marketing applications for brand-name and generic drugs, biological and biosimilar products, and medical devices. In addition to titles that reauthorize the four user fee programs (drugs, devices, generic drugs, and biosimilars) through FY2022, FDARA includes titles that

- modify the drug and device regulatory processes to encourage the development of drugs and devices for pediatric use;
- amend the law regarding medical device, prescription drug, and generic drug regulation; and
- make changes in several cross-cutting areas, such as annual reporting on inspection and analysis of use of funds.

The passage of the 21st Century Cures Act (P.L. 114-255) in December 2016 made numerous changes to the FDA approval processes for drugs, devices, and biologics, as well as other reforms to FDA; therefore, fewer non-user fee provisions were included in FDARA.

This report presents an overview of FDARA by title and section, providing a narrative context for each title, as well as a brief description of each section.

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Introduction

Food and Drug Administration (FDA) review of medical products (human drugs and devices) is funded through a combination of annual discretionary appropriations from Congress (budget authority) and user fees collected from industry. The human medical product user fee programs require reauthorization every five years to continue uninterrupted. Prior to the passage of the Food and Drug Administration Reauthorization Act of 2017 (FDARA, P.L. 115-52),[1] these programs were set to expire on September 30, 2017. The reauthorization legislation typically includes additional provisions related to FDA, since for many the bill is considered "must-pass" legislation in order for FDA product review activities to continue uninterrupted; as in prior reauthorizations, Congress made this user fee legislation a vehicle for addressing other FDA-related issues.[2] FDARA continues the five-year reauthorization cycle of the human medical product user fee programs, which allows FDA to continue collecting fees and using the revenue to support, among other things, the review of marketing applications for brand-name and generic drugs, biological and biosimilar products, and medical devices. In addition to titles that reauthorize the drug, device, generic drug, and biosimilar biological product user fee programs through FY2022, FDARA includes titles that

- modify the drug and device regulatory processes to encourage the development of drugs and devices for pediatric use;
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- make changes in several cross-cutting areas, such as annual reporting on inspection and analysis of use of funds.

The passage of the 21st Century Cures Act (P.L. 114-255) in December 2016 resulted in numerous changes to the FDA approval processes for drugs, devices, and biologics, as well as other reforms to FDA.[3] Therefore, fewer non-user fee provisions were included in FDARA.

FDARA has nine titles, as listed in **Table 1**. 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 makes modifications to facilitate the development and approval of drugs and devices for pediatric populations. Title VI addresses various aspects of prescription drug regulation, including drug supply chain security and expanded access, among other topics. Title VII makes modifications to the device inspection and approval processes. Title VIII makes modifications to improve patient access to generic drugs. Finally, Title IX covers annual reporting on inspections, performance reporting requirements, and analysis of use of funds, among other topics.

Table 1. Titles in FDARA

Title I	Fees Relating to Drugs
Title II	Fees Relating to Devices

[1] FDARA does not actually reauthorize the agency; instead, it reauthorizes each of four medical product user fee programs.

[2] See, for example, the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA, P.L. 112-144) and the Food and Drug Administration Amendments Act of 2007 (FDAAA, P.L. 110-85).

[3] For more information about Division A of the 21st Century Cures Act, see CRS Report R44720, *The 21st Century Cures Act (Division A of P.L. 114-255)*.

Title III	Fees Relating to Generic Drugs
Title IV	Fees Relating to Biosimilar Biological Products
Title V	Pediatric Drugs and Devices
Title VI	Reauthorizations and Improvements Related to Drugs
Title VII	Device Inspection and Regulatory Improvements
Title VIII	Improving Generic Drug Access
Title IX	Additional Provisions

Source: FDARA, P.L. 115-52.

This report presents an overview of FDARA by title and section, providing a narrative context for each title,[4] as well as a brief description of each section. There is generally one bullet for each section, and the FDARA section number is listed after the bullet in parentheses. For lengthy sections with multiple subsections, the FDARA section number and subsection are listed after the bullet in parentheses. Where relevant, the Federal Food, Drug, and Cosmetic Act (FFDCA) section being amended by the FDARA section is noted either in the introductory text or in the bulleted text.

Title I: Fees Relating to Drugs

FDARA Title I, the Prescription Drug User Fee Amendments of 2017, reauthorizes the prescription drug user fee program through FY2022.

FDARA reauthorizes the prescription drug user program for another five years, from FY2018 through FY2022. With the Prescription Drug User Fee Act (PDUFA) 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] For PDUFA to succeed, FDA, industry, and Congress had to agree 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

[4] All titles have a narrative overview with the exception of Titles VI and IX, because the topics covered by the provisions within those titles are too disparate to craft a coherent overview narrative.

[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, P.L. 110-85, P.L. 112-144, and, now, P.L. 115-52. For discussions of PDUFA, see CRS Report R44864, *Prescription Drug User Fee Act (PDUFA): 2017 Reauthorization as PDUFA VI* and CRS Report RL33914, *The Prescription Drug User Fee Act: History Through the 2007 PDUFA IV Reauthorization*.

authority regarding the regulatory review of other medical products.[6] User fees made up 41% of the FY2017 FDA budget.[7,8]

Following the precedent set by PDUFA, the user fee programs addressed in this legislation include both (1) legislation and (2) performance goal 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."[9] Congress has used the reauthorization process to expand 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 newer category of biosimilar biological products).[10]

Each five-year reauthorization sets a total amount of fee revenue for the first year and provides a formula for annual adjustments to that total based on inflation and workload changes. Until now (PDUFA I through V), PDUFA had required that three types of fees each contribute one-third of the fee revenue every year: application fees, establishment fees, and product fees.[11]

In general, FDARA Title I, the Prescription Drug User Fee Amendments of 2017 (commonly referred to as PDUFA VI), makes the following amendments to FFDCA Sections 736 and 736B:

- Establishes a new user fee structure to include a *program fee*, eliminating the establishment and product fees from earlier versions of PDUFA; continues the *application fee*, while eliminating the fee for a supplemental application (§102(a)).
- Provides that of the total prescription drug user fee revenue to be collected each year, 80% is to come from *program fees* and 20% is to come from *application fee*; establishes the annual base revenue and specifies additional dollar amounts for each of FY2018 through FY2022 (§102(b)).
- Modifies the inflation adjustment calculation; replaces the workload adjustment with a capacity planning adjuster; eliminates the final year adjustment provisions;

[6] For example, the Medical Device User Fee and Modernization Act (MDUFMA) and its reauthorization are in P.L. 107-250 and P.L. 110-85. For discussions of these user fee programs, see CRS Report R42130, *FDA Regulation of Medical Devices*.

[7] CRS Report R44576, *The Food and Drug Administration (FDA) Budget: Fact Sheet*.

[8] For a discussion of funding for the other three medical product user fee programs, see CRS Report R44750, *FDA Medical Product User Fee Reauthorization: In Brief*.

[9] FFDCA §735(6) [21 U.S.C. 379g (6)] defines the "process for the review of human drug applications" to include activities 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; monitoring of research conducted in connection with the review of human drug applications; and postmarket safety activities, including adverse event data collection systems and development of analytical tools, and enforcement of study and label-change requirements.

[10] For a more complete description of current law and discussion of issues relating to the Prescription Drug User Fee Act, see CRS Report R44864, *Prescription Drug User Fee Act (PDUFA): 2017 Reauthorization as PDUFA VI*.

[11] PDUFA V required three types of fees: (1) application fee—a drug's sponsor (usually the manufacturer) would pay a fee for the FDA review each time the manufacturer submitted a new drug application or supplemental application, or a biologics license application; (2) establishment fee—each manufacturer would pay an annual fee for each of its manufacturing establishments; and (3) product fee—each manufacturer would pay an annual fee for each product that fit within PDUFA's definition.

establishes an annual operating reserve adjustment; and establishes an additional direct cost adjustment (§102(c)).[12]

- Continues the requirement that the Secretary of Health and Human Services (HHS) establish and publish fees before the start of each fiscal year (§102(c)).
- Continues to require the Secretary to waive or reduce a fee (1) to protect the public health, if the fee would present a significant barrier to innovation, or (2) for the first human drug application from a small business; eliminates the authority of the Secretary to waive or reduce a fee because the fee would exceed the anticipated present and future costs of the review (§102(d)).
- Continues to consider an application or supplemental application to be incomplete until all required fees (now the application and program fees) have been paid (§102(e)).
- 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, (1) 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 (2) 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 (§102(f)).
- Continues to allow for the early payment of authorized fees (§102(g)).
- Continues the requirement for annual performance and fiscal reports (§103).
- Authorizes these prescription drug user fees from October 1, 2017, through September 30, 2022 (§§104 and 105).
- Includes a savings clause noting that fees for applications accepted by FDA for filing on or after October 1, 2012, but before October 1, 2017, will remain as under prior law (§106).

Title II: Fees Relating to Devices

FDARA Title II, the Medical Device User Fee Amendments of 2017, reauthorizes the medical device user fee program through FY2022.

Medical devices include a wide range of products 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 them in the United States. Congress gave FDA the authority to collect fees from the medical device industry in 2002.[13] User fees and direct appropriations from

[12] The total revenue under PDUFA VI for each of the fiscal years FY2018 though FY2022 is set to equal to the sum of (1) the annual base revenue ($878.6 million) for the fiscal year; (2) the dollar amount equal to the inflation adjustment for the fiscal year; (3) the dollar amount equal to the capacity planning adjustment for the fiscal year; (4) the dollar amount equal to the operating reserve adjustment for the fiscal year, if applicable; (5) the dollar amount equal to the additional direct cost adjustment for the fiscal year; and (6) the additional dollar amounts specified for each fiscal year (for each of FY2018 through FY2022, rounded to $20 million, $21 million, $17 million, $5 million, and $3 million, respectively).

[13] 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;

Congress fund FDA's review of medical devices. The user fees support FDA's medical device premarket review program to help reduce the time it takes the agency to review and decide 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.[14]

In general, Title II, the Medical Device User Fee Amendments of 2017 (MDUFA), makes the following amendments to FFDCA Sections 738 or 738A (titles that amend a different FFDCA section are noted):

- Adds a definition for the term "de novo classification request" (§202).[15]
- Changes the fee for a premarket notification submission, also called a 510(k) submission, from 2.0% of the premarket application (PMA) fee to 3.4% of the PMA fee; adds a new fee for a de novo classification request equal to 30% of the PMA fee; adds that no fee would be required for a de novo classification request if the device is intended solely for a pediatric population (§203(a)).
- Sets for each fiscal year the PMA fee amounts, which start at $294,000 per application in FY2018 and increase to $329,000 in FY2022, and annual establishment fee amounts, which start at $4,375 per manufacturing establishment in FY2018 and increase to $4,978 in FY2022; sets the total fee revenue amounts for each fiscal year, which start at $183,280,756 in FY2018 and increase to $213,687,660 in FY2022 (§203(b)).
- Allows for adjustment of the total revenue amounts by a specified inflation adjustment, with PMA and establishment fees adjusted accordingly (§203(c)).[16]
- Adds that a small business may pay 25% of the fee established for a de novo classification request (§203(d)).
- Changes the fee paid by small businesses for a premarket notification submission, also called a 510(k) submission, from 50% of the standard fee to 25% of the standard fee (§203(e)).
- Repeals FFDCA Section 738(f), which allowed for the waiver or reduction of a PMA fee or establishment fee if in the interest of public health (§203(f)).[17]

P.L. 108-214) and the Medical Device User Fee Stabilization Act of 2005 (MDUFSA; P.L. 109-43).

[14] For a more complete description of the MDUFA program, see CRS Report R44517, *The FDA Medical Device User Fee Program: MDUFA IV Reauthorization*.

[15] Under the FFDCA, novel devices lacking a legally marketed predicate are automatically designated Class III. FDAMA amended FFDCA Section 513(f) to allow FDA to establish a new, expedited mechanism for reclassifying these devices based on risk—the denovo 510(k)—thus reducing the regulatory burden on manufacturers. The de novo 510(k), though requiring more data than a traditional 510(k), often requires less information than a premarket approval (PMA) application. Section 202 defines a classification request under this provision.

[16] "[A]llows FDA to collect inflation-adjusted base fee amounts without any reduction in fees in the event that submission or registration volumes are higher than planned. Any further adjustments beyond inflation would only be necessary if projected submission volumes decrease or registrations fall below projections such that base fee amounts would need to be increased in order to generate the authorized total fee revenue in a given year." *Summary of Draft Recommended Changes to Statutory Language for MDUFA IV*, October 25, 2016, p. 3, at https://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM526532.pdf.

[17] Authority for the fee waiver and reduced fees was scheduled to end on October 1, 2017. The waivers and fee reductions had to be less than 2% of total fee revenue for that year. The fee waiver and reduced fees were intended for laboratory-developed test (LDT) manufacturers.

- Adds that failure to pay the fee associated with a de novo classification request shall be considered incomplete and will result in no acceptance of any and all subsequent submissions until all fees owed have been paid (§203(g)).
- Changes the specified amount for the "trigger" from $280,587,000 to $320,825,000 (§203(h)).[18]
- Strikes paragraph 4 of FFDCA redesignated Section 738(h), which had provided a fifth-year fee offset (§203(i)).[19]
- Continues the requirement for annual performance and fiscal reports (§204).
- Adds to FFDCA Section 514 a new subsection (d), which requires the Secretary to issue guidance and establish a pilot program under which testing laboratories may be accredited to assess whether a device conforms to established performance standards that have been accepted by the Secretary to demonstrate such conformity; requires an annual report on the progress of the pilot program to be posted on the FDA website; authority for the program sunsets on October 1, 2022 (§205).
- Amends FFDCA Section 523 regarding the scope of the third-party review program to specify in more detail that certain devices—such as "breakthrough devices" or any device intended to be permanently implantable or life-sustaining or life-supporting—may not be reviewed by an accredited person under the third-party review program; directs the Secretary to issue guidance on devices eligible for review under the program and factors in determining eligibility, and to post a list of eligible and ineligible devices on the FDA website; strikes a requirement to include details about this program in an FDA annual report (§206).[20]
- Amends FFDCA Section 745A, Electronic Format for Submissions, providing FDA with the authority to develop and implement device presubmissions and submissions solely in electronic format following the issuance of draft guidance (no later than October 1, 2019) and final guidance one year after the close of the public comment period on the draft guidance (§207).
- Includes a savings clause noting that fees for applications accepted by FDA for filing before October 1, 2017, will remain as under prior law (§208).
- Makes effective the amendments in Title II as of October 1, 2017, and authorizes the medical device user fees from October 1, 2017, through September 30, 2022 (§§209 and 210).

[18] To ensure that user fees supplement rather than replace congressional appropriations, this reauthorization 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 an amount specified in law.

[19] The fifth-year fee offset provision was eliminated because the MDUFA IV "negotiated fee setting structure allows FDA to collect and use inflation-adjusted base fee amounts each year without any reduction in fees due to increased submission or registration volume. Deleting the fee offset provision is necessary to implement the negotiated fee setting structure." *Summary of Draft Recommended Changes to Statutory Language for MDUFA IV*, October 25, 2016, pp. 3-4, at https://www.fda.gov/downloads/ForIndustry/UserFees/MedicalDeviceUserFee/UCM526532.pdf.

[20] The FDA annual report is required under FFDCA §1003(g).

Title III: Fees Relating to Generic Drugs

FDARA Title III, the Generic Drug User Fee Amendments of 2017, reauthorizes the generic drug user fee program through FY2022.

The Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act," P.L. 98-417) established an expedited pathway for generic drugs, allowing generic drug companies to submit an abbreviated new drug application (ANDA) to FDA for premarket review.[21] Instead of replicating animal and clinical research, the ANDA sponsor establishes that the generic product is the same as the brand drug,[22] thereby relying on the agency's determination that the brand drug is safe and effective.

While the Hatch-Waxman Act has been considered successful in increasing generic drug competition, the law has increased the number of generic drug submissions and thus FDA's workload, resulting in delayed approval of generic drug applications.[23] In March 2012, the median review time for generic drug applications was approximately 31 months, and FDA had a backlog of over 2,500 ANDAs.[24] In addition, as the number of manufacturing facilities increased, particularly foreign facilities, FDA had to conduct more inspections.[25]

To expedite ANDA reviews and bring uniformity to inspection schedules, Congress passed the Generic Drug User Fee Amendments (GDUFA, now called GDUFA I), which authorized FDA to collect fees from industry for agency activities associated with generic drugs. A May 2017 Government Accountability Office (GAO) report found that under GDUFA I, "the average time for FDA to complete the first review cycle decreased from 26 months for ANDAs submitted in fiscal year 2013 to about 14 months for those submitted in fiscal year 2015.... As of December 31, 2016, FDA had also acted on 89 percent of all ANDAs submitted in fiscal year 2015 within 15 months of receipt, exceeding its GDUFA [I] goal of acting on 60 percent of ANDAs received in fiscal year 2015 within 15 months."[26] The report also states that "as of December 31, 2016, FDA had acted on 92 percent of the 4,743 applications in the backlog pending review as of October 1, 2012, exceeding its GDUFA [I] goal of acting on 90 percent of such applications before the end of fiscal year 2017."[27]

In general, Title III, Fees Relating to Generic Drugs, makes the following amendments to FFDCA Sections 744A, 744B and 744C:

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[21] See CRS Report R44703 *Generic Drugs and GDUFA Reauthorization: In Brief*.

[22] The applicant must demonstrate that the generic drug is pharmaceutically equivalent (e.g., has the same active ingredient[s], strength, dosage form, route of administration) and bioequivalent to the brand-name product, among meeting other requirements (e.g., reviews of chemistry, manufacturing, controls, labeling, and testing).

[23] Statement of Janet Woodcock, M.D., Director, Center for Drug Evaluation and Research (CDER), FDA, before the Committee on Health, Education, Labor, and Pensions, United States Senate, "FDA User Fee Agreements: Strengthening FDA and the Medical Products Industry for the Benefit of Patients," March 29, 2012, http://www.fda.gov/NewsEvents/Testimony/ucm297390.htm.

[24] Ibid.

[25] Ibid.

[26] U.S. Government Accountability Office, Generic Drug User Fees: Application Review Times Declined, but FDA Should Develop a Plan for Administering Its Unobligated User Fees, GAO-17-452, May 2017, https://www.gao.gov/assets/690/685453.pdf.

[27] Ibid.

- Modifies the definition of *abbreviated new drug application* by excluding an application submitted by a state or federal governmental entity for a drug that is not distributed commercially (§302).
- Adds a definition for the term *contract manufacturing organization facility* (§302).
- Establishes a sunset date of October 1, 2022, for the one-time backlog fee paid by sponsors of currently pending applications (§303(a)).
- Creates a new *generic drug applicant program fee* (tiered based on the number of approved ANDAs an applicant owns), to be paid annually, and eliminates the prior approval supplement (PAS) fee. Continues the *drug master file* (DMF) *fee* but makes changes to the fee due date. Continues the *application filing fee* (for an ANDA) but makes changes to the refunding of ANDA fees in certain specified situations. Continues the *facility fee* (for generic drug facilities, active pharmaceutical ingredient [API] facilities, and contract manufacturing organization [CMO] facilities), but fees would not be required if the application is pending (§303(a)).
- Sets the total fee revenue for FY2018 at $493,600,000 and specifies the amount to be derived from each fee type: 35% from the new generic drug applicant program fees, 33% from ANDA fees, 5% from DMF fees, 20% from generic drug facilities, and 7% from API facilities. Specifies that fees for foreign generic drug and API facilities will be $15,000 higher than for domestic facilities and that the facility fee for a CMO is equal to one-third of the fee for a non-CMO facility (§303(b)).
- Makes minor changes to the annual inflation adjustment and the final year adjustment (§303(c)).
- Adds that information about whether a facility is a CMO must be included with the annual submission to the Secretary regarding identification of facilities (§303(e)).
- Adds that if a generic drug applicant program fee is not paid, then the applicant's name will be placed on a publicly available arrears list, any ANDA submitted by the applicant shall not be received by the Secretary, and all drugs marketed pursuant to any ANDA held by the applicant shall be deemed misbranded until the generic drug applicant program fee is paid (§303(f)).
- To ensure that user fees supplement rather than replace congressional appropriations, continues the requirement ("trigger") 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 (§303).
- Continues the requirement for annual performance and fiscal reports and adds reporting requirements (§304).
- Authorizes generic drug user fees from October 1, 2017, through September 30, 2022 (§§305 and 306).
- Includes a savings clause noting that fees for applications accepted by FDA for filing on or after October 1, 2012, but before October 1, 2017, will remain as under prior law (§307).

Title IV: Fees Relating to Biosimilar Biological Products

FDARA Title IV, the Biosimilar User Fee Amendments of 2017, reauthorizes the biosimilar biological product user fee program through FY2022.

A biosimilar is a biological product that is highly similar to a brand-name (innovator) biological product made by a pharmaceutical or biotechnology company.[28] A biological product, or biologic, is a preparation, such as a drug or a vaccine, made from living organisms. Unlike chemical drugs, which have a relatively simple structure and method of manufacture, biosimilars, with their more complex nature and method of manufacture, are not identical to a 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.

The Biologics Price Competition and Innovation Act of 2009 (BPCIA), enacted as Title VII of the Patient Protection and Affordable Care Act of 2010 (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 the pathway 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 demonstrating that it is highly similar to a biological product already allowed on the market by FDA. The Biosimilar User Fee Act of 2012 amended the FFDCA to provide FDA with the authority to collect use fees associated with the review of biosimilars.[29]

In general, Title IV, the Biosimilar User Fee Amendments of 2017 (BsUFA), makes the following amendments to FFDCA Sections 744G, 744H, and 744I:

- Adds a definition for the term "adjustment factor" and amends the definition for the term ''biosimilar biological product'' (§402).
- Adds that under certain specified conditions, a written request from a product sponsor for a refund of an annual biosimilar biological product development fee may be submitted to the Secretary not later than 180 days after the marketing application for the product is accepted for filing; removes the supplement fee; changes the application fee by no longer reducing the application fee by the cumulative amount of previously paid fees for the product; and removes the establishment fee and replaces it with a new biosimilar biological product program fee stipulating that product sponsors shall not be assessed more than five

[28] 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 a follow-on biologic is sometimes referred to as a biogeneric or generic biologic, the FDA and many others consider the use of the word *generic* to be inaccurate, both because the term *generic* in the context of chemical drugs means identical and a because biosimilar is not identical to the brand-name product. The FDA often uses the term *follow-on protein product*, because many biologics are proteins.

[29] For further information, see CRS Report R44620, *Biologics and Biosimilars: Background and Key Issues*.

biosimilar biological product program fees for a fiscal year per application (§403(a)).

- Sets the total fee revenue amount for FY2018 at $45,000,000; changes the allocation of the total revenue amount for a fiscal year among the various biosimilar fees; specifies that the initial biosimilar biological product development fee for a fiscal year shall be equal to the annual biosimilar biological product development fee for that fiscal year; specifies that the reactivation fee for a fiscal year shall be equal to twice the amount of the annual biosimilar biological product development fee for that fiscal year; and specifies that amounts of all biosimilar fees will be determined by the Secretary, except that after FY2018, any biosimilar fee will not be higher than 125% of the fee amount in FY2018 until the capacity planning adjustment is available (§403(b)).
- Establishes that the total revenue amounts for FY2019 through FY2022 will be based on a specified formula that takes into account the annual base revenue for the fiscal year, a new inflation adjustment, a new capacity planning adjustment, and the operating reserve for the fiscal year; the total amount for FY2018 may be adjusted to reflect updated workload estimates, but the adjustment may not exceed an increase of $9,000,000 (§403(c)).
- Allows the spending trigger requirements to be considered met in any fiscal year if the costs funded by budget authority are not more than 15% below the inflation adjusted amount for that year; the spending trigger will remain $20 million, adjusted for inflation (§403(f)).
- Continues requirements for performance reports and fiscal reports; drops the requirement for an independent accounting or consulting firm study of the workload volume and costs associated with the review of biosimilar biological product applications (§404).
- Authorizes these biosimilar biological product user fees from October 1, 2017, through September 30, 2022 (§§405 and 406).
- Includes a savings clause noting that fees for applications accepted by FDA for filing before October 1, 2017, will remain as under prior law (§407).

Title V: Pediatric Drugs and Devices

Title V of FDARA makes modifications to facilitate the development and approval of drugs and devices for pediatric populations.

Medical product manufacturers may be reluctant to test drugs and medical devices in children because of economic, ethical, legal, and other obstacles.[30] Congress has acted to incentivize such testing. Current programs stem from the Best Pharmaceuticals for Children Act (BPCA),[31] the

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

[31] Congress, in the Food and Drug Administration Modernization Act of 1997 (FDAMA, P.L. 105-115), provided an incentive in the form of a six-month extension of regulatory exclusivity to drug manufacturers that completed pediatric studies requested by the FDA. This incentive was authorized for five years. Congress passed the Best Pharmaceuticals for Children Act of 2002 (BPCA, P.L. 107-109) to reauthorize the six-month exclusivity provision, continuing the incentive to manufacturers to conduct pediatric-specific research. Congress reauthorized BPCA as part of the Food and

Pediatric Research Equity Act (PREA),[32] and the Pediatric Medical Device Safety and Improvement Act (PMDSIA).[33]

BPCA provides an incentive in the form of a six-month extension of regulatory exclusivity for a drug whose manufacturer completes FDA-requested pediatric studies. PREA requires pediatric assessments to support pediatric use information in product labeling. PMDSIA requires certain reports for pediatric medical devices, provides incentives for manufacturers to create pediatric medical devices, and gives FDA the authority to require postmarket studies of approved pediatric devices to ensure their continued efficacy and safety.

Prior to the enactment of the incentive provisions in 1997, more than 80% of approved drugs contained no pediatric-specific labeling information. Since then, there have been more than 600 approved labeling changes with pediatric-specific information, 149 of which were completed following FDASIA.[34] BPCA and PREA studies have resulted 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. However, gaps continue to exist, especially for pediatric cancer, with FDA noting that because children's cancers often occur in different organs than adult cancers, manufacturers are able to obtain a waiver from PREA requirements.[35]

PMDSIA added an annual reporting requirement to Congress on pediatric medical devices, including the number of pediatric device approvals per year and the review time for these devices. In August 2017, FDA published the seventh report pursuant to this requirement.[36]

In general, Title V, Pediatric Drugs and Devices, makes the following amendments:

- Amends PHSA Section 409I(a)(2)(A)(ii) to require the Secretary, in developing the list of priority issues in pediatric therapeutics that require study, to consider where identification of biomarkers for particular pediatric diseases, disorders, or conditions may be beneficial in pediatric populations (§501).
- Amends PHSA Section 409I(c)(6) to require that reports on pediatric studies completed in accordance with an award under this section be posted on the National Institutes of Health (NIH) website, as specified, and that any interested person be allowed to submit comments on these studies to the FDA Commissioner and eliminates the requirement that the Secretary publish in the *Federal Register* summaries of reports that request a labeling change (§501).
- Amends PHSA Section 409I(d) to reauthorize the appropriation of $25 million for each of FY2018 through FY2022 for the program for pediatric studies of drugs at NIH (§501).

Drug Administration Amendments Act (FDAAA, P.L. 110-85) and made it permanent with the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-114).

[32] PREA was established by P.L. 108-155 and, along with BPCA, was made permanent by FDASIA (P.L. 112-144).

[33] PMDSIA was enacted in Title III of the Food and Drug Administration Amendments Act of 2007 (FDAAA, P.L. 110-85). FDASIA Section 620 amended FDAAA Section 305(e) to reauthorize the demonstration grant program for improving pediatric device availability, and to authorize the appropriation of $5.25 million for each of FY2013 through FY2017.

[34] FDA, "Best Pharmaceuticals For Children Act and Pediatric Research Equity Act," July 2016, Report to Congress, https://www.fda.gov/downloads/scienceresearch/specialtopics/pediatrictherapeuticsresearch/ucm509815.pdf.

[35] Ibid.

[36] FDA, "FY2016 Premarket Approval of Pediatric Uses of Devices," https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/UCM572980.pdf.

- Amends FFDCA Section 515A(a)(3) to add additional elements to the required annual report on pediatric medical devices; amends Section 305(c) of FDAAA to require a nonprofit consortium that receives a demonstration grant to provide regulatory consultation to device sponsors in support of a pediatric device application, where appropriate, and continues previously required consortium activities; amends Section 305(e) of FDAAA to reauthorize the appropriation of $5.25 million for FY2018 through FY2022 for the demonstration grant program for improving pediatric medical devices; and requires the Secretary to convene a public meeting on the development, approval or clearance, and labeling of pediatric medical devices not later than one year after enactment and to include a summary of the meeting in the report required under FFDCA Section 515A(a)(3) (§502).
- Amends FFDCA Section 505B(e)(2)(C) regarding meetings the Secretary is required to hold with a sponsor: requires the Secretary to meet with the sponsor of an application for a drug to treat a serious or life-threatening disease to discuss preparation of the initial pediatric study plan no later than the end-of-Phase 1 meeting or within 30 calendar days of request receipt, whichever is later; for applications for other drugs, continues the requirement that the meeting be as soon as practicable, but within 90 days of the receipt of the pediatric study plan; and requires a meeting "to discuss the bases for deferrals or waivers" (§503).
- Amends FFDCA Section 505B to require the sponsor of an original application for a new active ingredient, including an orphan drug, that is intended to treat an adult cancer and is directed at a molecular target that the Secretary determines is "substantially relevant to the growth or progression of a pediatric cancer" to conduct specified pediatric studies and make specified reports on the required investigation (§504).
- Requires the Secretary to publish on the FDA website and update regularly a list of molecular targets the Secretary determines, in consultation with the National Cancer Institute and two specified FDA committees, to be "substantially relevant to the growth or progression of a pediatric cancer" and that may trigger the new study requirements, as well as a list of molecular targets for which the pediatric study requirements will be automatically waived (§504).
- Requires the Secretary to convene a public meeting with specified stakeholders to inform development of guidance on implementation of the requirements surrounding molecularly targeted cancer drugs; requires the Secretary to issue final guidance on this implementation; modifies the contents of the report on pediatric assessments that the Secretary is required to submit to Congress every five years;[37] and requires GAO to study and report to the authorizing congressional committees on the effectiveness of the new pediatric assessment and investigation requirements on the development of drugs and biologics for pediatric cancer indications (§504).
- Amends FFDCA Section 505A to require the Secretary to review and act on a proposed pediatric study request or proposed amendment to a written request within 120 days of submission, and to provide to the internal review committee any response to a proposed pediatric study request. Directs the Secretary, acting

[37] Section 508 of FDASIA required the Secretary to report to Congress by July 9, 2016, and every five years thereafter, on various activities related to pediatric assessments under FFDCA Sections 505A and 505B.

through the internal review committee, to develop and implement a plan to achieve earlier submission of pediatric studies under the BPCA (§505).

- Amends the BPCA to permanently authorize the requirement that at least one individual in FDA's Office of Pediatric Therapeutics has expertise in neonatology and requires the Secretary to issue draft guidance on clinical pharmacology considerations for neonatal studies for drugs and biologics (§505).
- Amends FFDCA Section 505B(d) to require the Secretary to inform the Pediatric Advisory Committee of correspondence about noncompliance with required assessments; amends FFDCA Section 505C to require that the FDA internal committee for the review of pediatric plans and other materials include expertise in "pediatric rare diseases"; and requires the Secretary to submit to Congress and post on the FDA website a report on the lack of information in the labeling for pediatric use of drugs for indications with orphan designations (§505).

Title VI: Reauthorizations and Improvements Related to Drugs

FDARA includes 11 other provisions that address reauthorizations, drug supply chain security, pediatric labeling, and expanded access, among other things.

In general, Title VI, Reauthorization and Improvements Related to Drugs, makes the following amendments:

- Amends FFDCA Section 505(u) to extend until October 1, 2022, the period during which a manufacturer may elect to consider, in an application for approval under FFDCA Section 505(b), a single enantiomer (each of a pair of molecules that are mirror images of one another) that is also in an approved racemic (having both the left- and right-handed molecular forms of an active ingredient) drug as a separate active ingredient (§601).
- Amends FFDCA Section 566(f) to reauthorize 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 FY2018 through FY2022 (§602).
- Amends Section 5(c) of the Orphan Drug Act to reauthorize the appropriation of $30 million for each of FY2018 through FY2022 for grants and contracts to defray the costs of qualified testing used for orphan drug development (§603).
- Amends FFDCA Section 801(d) to prohibit importation of a foreign-made drug, with certain exceptions, unless it is authorized to be marketed in the United States and labeled accordingly (§604).
- Amends FFDCA Section 303(b) to specify an increased penalty for making, selling, or dispensing a counterfeit drug (§604).
- Amends FFDCA Section 569C(c) to change the definition of "patient experience data" in the context of required strategies to solicit patients' views during the medical product development process to include data intended to provide

information about patients' experiences with a disease or condition or a related therapy or clinical investigation (§605).

- Amends FFDCA Section 505-1(e) to allow the Secretary to require, as part of a Risk Evaluation and Mitigation Strategies (REMS) communication plan, the manufacturer to disseminate to health care providers information about drug formulations or properties, including the limitations of those properties and how they may be related to serious adverse effects (§606).
- Amends FFDCA Section 527 to require an applicant, in order to obtain the seven-year orphan drug exclusivity for a drug that is the same drug for the same disease or condition as a previously approved drug, to demonstrate that its product is *clinically superior*, meaning that "the drug provides a significant therapeutic advantage over and above an already approved or licensed drug in terms of greater efficacy, greater safety, or by providing a major contribution to patient care" (§607).
- Amends FFDCA Section 505A(o) to expand the circumstances under which certain patent- and exclusivity-protected pediatric information may be omitted from drug labeling to permit the approval of the drug for adult use to include 505(b)(2) new drug applications (NDAs);[38] expands the applicable categories of such exclusivity to include orphan drug, pediatric, and qualified infectious disease product exclusivity; and expands the circumstances under which the Secretary is allowed to require the applicant to include a disclaimer with respect to the omitted information (§608).
- Includes a Sense of Congress that the Secretary should commit to engaging with Congress to take action and enact legislation to lower the cost of prescription drugs for consumers while balancing the need to encourage innovation and increase competition in the pharmaceutical market (§609).
- Requires the Secretary to (1) through the FDA Commissioner and in coordination with the NIH Director and consultation with specified stakeholders (e.g., patients, health care providers), convene a public meeting to discuss clinical trial inclusion and exclusion criteria; (2) issue guidance on clinical trial eligibility criteria; (3) issue a publicly available report on the topics discussed at the meeting, as specified; and (4) acting through the FDA Commissioner, issue or revise guidance or regulations to streamline Institutional Review Board (IRB) review for individual patient expanded access protocols, and update any relevant forms associated with individual patient expanded access (§610).
- Requires GAO to report to Congress on individual access to investigational drugs through FDA's expanded access program, as specified (§610).
- Amends FFDCA Section 561A(f) to change the date by which a company must post on its website its expanded access policies to the earlier of the first initiation of a Phase 2 or Phase 3 study with respect to the investigational drug, or 15 days after the drug is designated as a breakthrough therapy, fast-track product, or regenerative advanced therapy (§610).
- Amends FFDCA Section 524(a)(4) to require that a *tropical disease product application* contains (1) reports of one or more new clinical investigations that

[38] A 505(b)(2) NDA is an NDA that contains full reports of investigations of safety and effectiveness, where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use (e.g., published literature).

are conducted or sponsored by the applicant and that are essential to approval, and (2) an attestation from the sponsor that such reports were not submitted as part of an application for approval or licensure in other countries, as specified, prior to September 27, 2007 (§611).

Title VII: Device Inspection and Regulatory Improvements

FDARA Title VII modifies the device inspection and approval processes.

Medical devices include a wide range of products 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.[39]

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 devices are class II; and (3) high-risk devices 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, manufactures may use two pathways 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 a 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 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 the device's 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.

In general, Title VII makes the following amendments to various FFDCA provisions to modify various aspects of device regulation:

- Amends FFDCA Section 510(h) to change the inspection schedule of establishments engaged in the manufacture or processing of a device from biennial to a risk-based approach (§701).

[39] For additional information, see CRS Report R42130, *FDA Regulation of Medical Devices*.

- Amends FFDCA Section 704 to require the Secretary to identify and adopt uniform standards and processes for the conduct of device establishment inspections, other than for-cause inspections; these must allow unspecified exceptions to the inspection processes and standards, require notification within a reasonable timeframe to the establishment of the type and nature of the inspection, and require to the extent feasible advance notice of the records that will be requested; and requires the issuance of draft and final guidance regarding these changes to inspections (§702).
- Amends FFDCA Section 501(j) to add that a device may be considered to be adulterated if the device establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection (§702).
- Amends FFDCA Section 704 to reauthorize through FY2022 the third-party inspection program, allowing accredited third parties to inspect medical device establishments (§703).
- Amends FFDCA Section 801 to make changes regarding the certification of devices for export: if a request for certification is denied, the basis for the denial shall be provided in writing; the Secretary shall not deny a request for certification solely on the basis of an inspection report that documents violations, provided that the device establishment has agreed to a plan of correction in response to such a report; the owner of a device establishment may request a review at any time to present new information that addresses the reasons for denial of certification; and requires the issuance of guidance regarding these changes (§704).
- Amends FFDCA Section 794(g) to allow the Secretary to recognize auditing organizations recognized by governmental organizations to facilitate international device establishment inspections (§705).
- Adds a new subsection (p) to FFDCA Section 520 regarding the approval, clearance, or classification of diagnostic imaging devices that use contrast agents; provides definitions for "applicable medical imaging device" and "contrast agent;" and specifies that the agency center that reviews devices has primary jurisdiction over such review (§706).
- Adds a new subsection (y) to FFDCA Section 505; following the marketing authorization of an imaging device that uses a contrast agent, the sponsor of the contrast agent may submit a supplemental application for the new use of the contrast agent; specifies that the agency center charged with the premarket review of drugs has jurisdiction over review of the supplement; and provides definitions for "new use," "applicable medical imaging device," and "contrast agent" (§706).
- Amends FFDCA Section 513 to make changes to the classification of accessories that are used with medical devices; directs the Secretary to classify an accessory to a device based on the risks of the accessory when used as intended, rather than the risk of the device with which the accessory is intended to be used (§707).
- Amends FFDCA Section 519 to direct the Secretary to initiate one or more voluntary postmarket pilot projects to generate timely and reliable information on the safety and effectiveness of approved or cleared medical devices: the pilot projects will use electronic health data and will prioritize certain specified devices and device types; requires the Secretary to submit annual reports to Congress on the status of each pilot project and sunsets the project on October 1,

2022; requires the Secretary, acting through the FDA Commissioner, to conduct a review through an independent third-party contract to determine whether such pilot projects generate reliable and timely evidence about the safety and effectiveness of medical devices (§708).

- Adds a new subsection (q) to FFDCA Section 520 regarding the regulation of over-the-counter hearing aids providing a definition of over-the-counter hearing aids and directing the Secretary to promulgate proposed regulations regarding over-the-counter hearing aids and to finalize such regulations, as specified; requires a determination on whether 510(k) premarket notification is necessary to provide reasonable assurance of safety and effectiveness of over-the-counter hearing aids; stipulates that state and local governments shall not establish or continue in effect any law or regulation that would restrict or interfere with the sale or use of over-the-counter hearing aids; requires the issuance of updated draft and final guidance clarifying which products meet the definition of a device and which products meet the definition of a personal sound amplification product as specified in the guidance; and requires the Secretary to submit a report to Congress analyzing any adverse events related to over-the-counter hearing aids (§709).
- Requires the Secretary, acting through the Commissioner of FDA, to post on the FDA website a report on the quality, safety and effectiveness of servicing medical devices (servicing is defined as "refurbishing, reconditioning, rebuilding, remarketing, repairing, remanufacturing, or other servicing of the device"); and specifies the report contents, including how the regulation of device servicing could be improved and any actions that could be taken to track adverse events caused by servicing errors (§710).

Title VIII: Improving Generic Drug Access

FDARA Title VIII modifies the generic drug regulatory process.

The Hatch-Waxman Act established an expedited pathway for generic drugs, allowing a generic company to submit an ANDA to FDA for premarket review. In the ANDA, the applicant must demonstrate that the generic product is the same as the brand-name drug or reference listed drug (RLD).[40] Generally, the brand-name drug is called the RLD because the generic product's ANDA refers to the clinical data in the brand-name drug's NDA. The *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") lists drugs approved by FDA on the basis of safety and effectiveness, as well as those drugs identified by FDA as eligible to be RLDs, among other things.[41]

Largely because a generic sponsor does not perform costly animal and clinical research—and usually does not pay for expensive advertising, marketing, and promotion—the generic drug company is able to sell its generic drug product at a lower price compared with the brand drug

[40] The applicant must demonstrate that the generic drug is pharmaceutically equivalent (e.g., has the same active ingredient[s], strength, dosage form, route of administration) and bioequivalent to the brand-name product, among meeting other requirements (e.g., reviews of chemistry, manufacturing, controls, labeling, and testing).

[41] FDA, Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"), https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm.

product. A 2016 report sponsored by the Generic Pharmaceutical Association (GPhA, renamed as the Association for Affordable Medicines [AAM]), states that generic drugs saved the U.S. health system $1.46 trillion from 2006 to 2015.[42] "Generics are 89% of prescriptions dispensed but only 27% of total drug costs. Put another way, brand drugs are only 11% of prescriptions but are responsible for 73% of drug spending."[43]

Because generic competition is associated with lower drug prices, some have looked to FDA to increase pharmaceutical competition, for example, by prioritizing the review of certain ANDAs. On June 27, 2017, FDA announced that the agency is taking steps to increase generic competition and facilitate market entry of lower-cost drugs.[44] Specifically, FDA posted on its website a list of drugs that have no listed patents or exclusivities and for which there is no approved ANDA. The agency states that it intends to expedite the review of ANDAs for drugs on this list and will continue to expedite the review of ANDAs until there are three approved generics for a given drug.

In general, Title VIII, Improving Generic Drug Access, makes the following amendments to various FFDCA provisions to modify aspects of generic drug regulation:

- Amends FFDCA Section 505(j) to require the Secretary to prioritize the review and act, within eight months of the submission date, on ANDAs submitted for drugs (1) with not more than three approved products listed in the Orange Book and for which there are no blocking patents and exclusivities and (2) on the FDA's drug shortage list (§801).
- Allows the Secretary to expedite the inspection or reinspection of an establishment that proposes to manufacture such a drug (§801).
- Requires the applicant, in order to qualify for priority review, to provide complete, accurate information regarding the facilities involved in manufacturing processes and testing of the drug to enable the Secretary to determine whether an inspection of the facility is necessary (§801).
- Requires the Secretary to publish on the FDA website, and update every six months, a list of drugs for which all patents and periods of exclusivity have expired and for which no ANDA has been approved (§801).
- Amends FFDCA Section 505(j), requiring the Secretary, upon request of the applicant, to provide review status updates for pending ANDAs, as specified (§802).
- Creates a new FFDCA Section 506H, "Competitive Generic Therapies" which allows the Secretary, upon request of the applicant, to designate a drug as a *competitive generic therapy* if the Secretary determines that there is *inadequate generic competition*; defines *inadequate generic competition* to mean there is not more than one approved drug listed in the active section of the Orange Book that is either (1) the RLD (i.e., the brand-name drug, and there is no approved generic) or (2) a generic drug with the same RLD as the drug seeking competitive

[42] The Generic Pharmaceutical Association, *2016 Generic Drug Savings & Access in the United States Report*, at http://www.gphaonline.org/media/generic-drug-savings-2016/index.html. This, the eighth annual report, was compiled by Quintiles IMS Institute for GPhA.

[43] Ibid.

[44] FDA, "FDA Tackles Drug Competition to Improve Patient Access," *FDA News Release*, June 27, 2017, https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/UCM564725.htm.

generic therapy designation (i.e., one generic drug has been approved, but the RLD has been discontinued);[45] and allows the Secretary to expedite the development and review of an ANDA of a competitive generic therapy (§803).

- Allows the Secretary, upon request of the applicant, to take certain actions to increase communication, such as holding meetings with the applicant and review team during drug development (§803).
- Requires the applicant to report to the Secretary on whether the drug designated as a competitive generic therapy has been marketed in interstate commerce (§803).
- Requires the Secretary to issue draft and final guidance specifying the process and criteria by which the Secretary designates a drug as a competitive generic therapy, among other things, and to issue or revise any regulations that may be necessary for carrying out this provision (§803).
- Creates a new FFDCA Section 506I, "Prompt Reports of Marketing Status" which requires the holder of an approved application to (1) notify the Secretary in writing before withdrawing an approved brand-name or generic drug from sale, either 180 days before doing so or as soon as practicable, (2) notify the Secretary within 180 days of approval if the drug will not be available for sale within 180 days of the date of approval and (3) review the information in the Orange Book and notify the Secretary in writing that either all of the application holder's drugs in the active section of the Orange Book are available for sale, or that one or more of the application holder's listed drugs have been withdrawn from sale or have never been available for sale; and requires each of these notifications to include specified information (e.g., drug identity, reason for withdrawal from sale) (§804).
- Allows the Secretary to move the application holder's drugs from the active section of the Orange Book to the discontinued section if the holder fails to submit the required information (§804).
- Requires the Secretary to report to Congress annually the number of pending suitability petitions[46] and the number of such petitions pending a substantive response for more than 180 days from the date of receipt (§805).
- Requires the Secretary to develop a protocol to expedite review of timely responses to inspection observations, address expedited reinspection, and establish a six-month timeline for completion of review and response to such reports; this protocol would apply to drug applications for which (1) approval depends on resolving the facility issues identified in the inspection report, (2) the facility issues are the only barrier to approval, and (3) the drug appears on the FDA shortage list or there are not more than three other approved ANDAs that reference the same listed drug and less than six tentatively approved ANDAs (§806).

[45] According to FDA draft guidance, "Where FDA cannot select a drug product approved under section 505(c) of the FD&C Act as the reference standard (e.g., where the RLD has been withdrawn from sale for reasons other than safety and effectiveness), FDA generally will select a previously approved ANDA that referred to the RLD as the reference standard." See, *Referencing Approved Drug Products in ANDA Submissions*, January 2017, https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536962.pdf.

[46] A suitability petition is submitted by an applicant requesting permission to submit an ANDA for a drug product that is not the same as a listed drug with respect to route of administration, dosage form, strength, or active ingredient.

- Requires the Secretary, not later than 180 days after enactment, to post on the FDA website a quarterly report on the number of pending ANDAs and priority review applications, as specified (§807).
- Amends FFDCA Section 505(j) to provide eligibility for a 180-day exclusivity period for an approved ANDA that is designated as a *competitive generic therapy* and for which there are no blocking patents or exclusivities, subject to forfeiture if the applicant fails to market the drug within 75 days of approval and adds definitions for the terms *competitive generic therapy* and *first approved applicant* (§808).
- Requires GAO to conduct a study on issues related to first cycle approvals of generic drugs, as specified, and to submit a report to the House Energy and Commerce and Senate HELP Committees describing its findings and conclusions (§809).

Title IX: Additional Provisions

FDARA includes five miscellaneous sections concerning technical corrections, an annual report on inspections, streamlining and improving consistency in performance reporting, analysis of the use of funds, and facilities management.

In general, these sections do the following:

- Make technical corrections to the 21st Century Cures Act (P.L. 114-225) and to Sections 506F, 506G, 510, 513, 515B, and 515C of the Federal Food, Drugs, and Cosmetics Act (§901).
- Require the Secretary to annually post on the FDA website specified information (including timing of actions) on facility inspections necessary for drug approval, device approval, and device clearance (§902).
- To streamline and improve consistency in performance reporting for the four human medical product user fee programs, amend FFDCA Sections 736B, 738A, 744C, and 744I to require specified quarterly posting on the FDA website and inclusion of additional material in the annual performance reports for each program; defines quarterly "real time reporting" to include specified information on draft and final guidance and public meetings; defines annual report information to include "data, analysis, and discussion" related to (1) changes in the hiring of full-time equivalents funded by user fee revenue and by budget authority, (2) "changes in the fee revenue amounts and costs for the process for the review of human drugs, including identifying drivers of such changes" and (3) other personnel data (§903).
- Amend FFDCA Section 736B to require the Secretary to quarterly post on the FDA website the number of NDAs and BLAs filed and the number approved (§903).
- Amend FFDCA Section 738A to require the Secretary to include in the annual MDUFA performance report the number of premarket applications filed, the number of 510(k) reports submitted, and the number of expedited development and priority review designations (§903).

- Amend FFDCA Section 744I to require the Secretary to include in the annual BsUFA performance report information on the progress of previous application cohorts, number of new applications filed and those approved, and number of resubmitted applications and those approved (§903).
- Amend FFDCA Sections 736B, 738A, 744C, and 744I to require, in the annual reports of each of the human medical product user fee programs, specified analyses of the use of funds to include information such as differences between aggregate numbers of applications and approvals, analysis of performance goals met and missed, and a determination of causes of ability to meet performance goals; and require the issuance of corrective action reports; and require enhanced communications with Congress and participation in congressional hearings (§904).
- Require GAO to (1) conduct a study, with specified content, on FDA expenses related to facility maintenance and renovation; and (2) report to the authorizing congressional committees on the study's results and recommendations (§905).
- Amend FFDCA Sections 736, 738, 744B, and 744H to limit the scope of allowed uses of user fee revenue for expenses related to things such as facilities, furniture, and supplies; beginning October 1, 2023, "leasing and necessary scientific equipment" will replace "leasing, maintenance, renovation, and repair of facilities and acquisition, maintenance, and repair of fixtures, furniture, scientific equipment, and other necessary materials and supplies" (§905).

Author Information

Amanda K. Sarata, Coordinator
Specialist in Health Policy

Judith A. Johnson
Specialist in Biomedical Policy

Agata Dabrowska
Analyst in Health Policy

Susan Thaul
Specialist in Drug Safety and Effectiveness

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