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Generic Drugs and GDUFA Reauthorization: In Brief

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Summary

A generic drug is a lower-cost copy of a brand-name chemical drug. Marketing of the generic drug becomes possible only when the brand-name—also called innovator—drug is no longer protected from market competition by patent and other protections, called regulatory exclusivity.

Prior to marketing, the sponsor of a brand-name drug must submit to the Food and Drug Administration (FDA) clinical data in a new drug application (NDA) to support the claim that the drug is safe and effective for its intended use. The FDA uses the information in the NDA as a basis for approving or denying the sponsor's application. Once a drug is approved, the brand-name manufacturer has free rein in setting the drug price due to a government-sanctioned monopoly for a defined period of time. This enables the company to recoup its research and development expenses, allow further R&D investment, as well as provide a profit to stock holders.

The branded drug is protected from market competition by (1) patents issued by the U.S. Patent Office and (2) regulatory exclusivity granted by the FDA following enactment of the Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417), also called the Hatch-Waxman Act. These congressionally established incentives allow the brand name company to charge a much higher price for the drug product than the cost of manufacture. In one extreme example, the annual price for a patient taking the cancer drug Gleevec would be $216—including a 50% profit—far lower than the current annual price of $107,799 in the United States.

The Hatch-Waxman Act amended the Federal Food, Drug, and Cosmetic Act (FFDCA) allowing a generic drug manufacturer to submit an abbreviated NDA (ANDA) to the FDA for premarket review. In the ANDA, the generic company establishes that its drug product is chemically the same as the already approved drug and thereby relies on the FDA's previous finding of safety and effectiveness for the approved drug. Because the 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 drug product at a lower price compared with the branded drug product. The cost of a generic drug is, on average, about 85% lower than the brand name product.

According to FDA, the success of the Hatch-Waxman Act led to significant regulatory challenges for the agency. FDA's resources did not keep pace with the increasing number of ANDAs, resulting in delayed approvals of generic drugs, "a major concern for the generics industry, FDA, consumers, and payers alike." In March 2012, median review time for generic drug applications was approximately 31 months and FDA had a backlog of over 2,500 ANDAs. In addition, FDA had to conduct more inspections as the number of manufacturing facilities grew, "with the greatest increase coming from foreign facilities."

To expedite ANDA reviews and provide resources for more inspections, FDA had proposed generic drug user fees in each annual budget request to Congress beginning with the FY2008 request. Such fees became possible when the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144) became law in July 2012. Title III of FDASIA, the Generic Drug User Fee Amendments (GDUFA), authorized FDA to collect fees from industry for agency activities associated with generic drugs. Under what is now called GDUFA I, such fees are allowed to be collected from October 2012 through September 2017.

Between October 2015 and August 2016, FDA held negotiation sessions with industry on GDUFA reauthorization. In October 2016, FDA posted on its website the draft agreement—GDUFA II—setting fees and FDA performance goals for FY2018 through FY2022. A final GDUFA II recommendation will be submitted to Congress by January 15, 2017.

Contents

Tables

Contacts

Introduction

A generic drug is a lower-cost copy of a brand-name chemical drug. Marketing of the generic drug becomes possible only when the brand-name—also called innovator—drug is no longer protected from market competition by patent and other protections, called regulatory exclusivity. Food and Drug Administration (FDA) approved generic drugs "have the same high quality, strength, purity and stability as brand-name drugs," and have met the same FDA standards regarding manufacturing, packaging, and testing as brand-name drugs.[1] Generic drugs are required to have the same active pharmaceutical ingredient (API) as the brand name product, but need not have the same inactive ingredients.[2]

Prior to marketing, the sponsor of a brand-name drug must submit to FDA clinical data in a new drug application (NDA) to support the claim that the drug is safe and effective for its intended use.[3] The FDA uses the information in the NDA as a basis for approving or denying the sponsor's application.

The Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417)—also called the Hatch-Waxman Act—amended the Federal Food, Drug, and Cosmetic Act (FFDCA) allowing a generic drug manufacturer to submit an abbreviated NDA (ANDA) to the FDA for premarket review.[4] In the ANDA, the generic company establishes that its drug product is chemically the same as the already approved drug and thereby relies on the FDA's previous finding of safety and effectiveness for the approved drug. The generic drug must also be bioequivalent to the brand-name drug, meaning it delivers "the same amount of active ingredients in the same amount of time as the brand-name drug."[5]

Because the generic sponsor does not perform costly animal and clinical research[6]—and usually does not pay for expensive advertising, marketing, and promotion—the generic drug company is

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[1] FDA, Understanding Generic Drugs, http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm.

[2] API is defined as "any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body." FDA, "Guidance for Industry, Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients," at http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm200364.htm#P1422_111232.

An inactive ingredient, or excipient, is intentionally added to therapeutic and diagnostic products, but is not intended to exert therapeutic effects at the intended dosage, although it may act to improve product delivery (e.g., enhance absorption or control release of the drug substance). Examples of excipients include fillers, extenders, diluents, wetting agents, solvents, emulsifiers, preservatives, flavors, absorption enhancers, sustained-release matrices, and coloring agents. FDA, "Guidance for Industry: Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients," at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079250.pdf.

[3] For a description of the new drug application and approval process, see CRS Report R41983, *How FDA Approves Drugs and Regulates Their Safety and Effectiveness*, by (name redacted)

[4] For further information on the Hatch-Waxman Act, see CRS Report R44643, *The Hatch-Waxman Act: A Primer*, by (name redacted), and CRS Report R41114, *The Hatch-Waxman Act: Over a Quarter Century Later*, by (n ame red acted) and (name redacted) .

[5] FDA, "FY2013 Performance Report to the President and Congress for the Generic Drug User Fee Amendments," pp. 1-2, at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/UCM384177.pdf.

[6] This requirement applies to drugs first marketed after 1962 following enactment of the Kefauver-Harris Drug Amendments (P.L. 87-781) to the Federal Food Drug and Cosmetic Act (FFDCA) in the wake of deaths and birth defects from the tranquilizer thalidomide marketed in Europe. For further information, see CRS Report R41983, *How* (continued...)

able to sell its generic drug product at a lower price compared with the brand drug product. FDA states that on average, "the cost of a generic drug is 80 to 85 percent lower than the brand name product."[7] According to a 2016 report sponsored by the Generic Pharmaceutical Association (GPhA), "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."[8] The 2016 GPhA report estimates the 10-year (2006-2015) savings from the use of generic drugs at $1.46 trillion.[9]

FDA Sources of Information on Generic Drugs

Drugs@FDA, a catalog of FDA-approved drug products and drug labeling information.

http://www.accessdata.fda.gov/scripts/cder/daf/

Electronic Orange Book, provides information on generic equivalents to brand name products.

http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm

First Generics, first approval by FDA permitting a manufacturer to market a generic drug in the United States.

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/ANDAGenericDrugApprovals/default.htm

Once a drug is approved, the brand-name manufacturer sets the drug price based on a number of factors. Patent and regulatory exclusivity allow the company to recoup its research and development expenses, allow further R&D investment, and provide a profit to stock holders. The branded drug is protected from market competition by (1) patents issued by the U.S. Patent Office and (2) regulatory exclusivity granted by the FDA following enactment of the Hatch-Waxman Act.[10] These incentives allow the brand name company to charge a much higher price for the drug product than the cost of manufacture. For example, the cancer drug Gleevec (imatinib) "can be sustainably and profitably produced at a price between $128 and $216 per person-year, which are far lower than the current prices of around $30,000 in EU and $107,799 per person-year in the USA."[11]

The price of a drug is strongly correlated with the number of different manufacturers marketing the drug. According to an FDA analysis, "the first generic competitor prices its product only

(...continued)

FDA Approves Drugs and Regulates Their Safety and Effectiveness, by (name redacted)

[7] FDA, Facts about Generic Drugs, at http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm.

[8] 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 on behalf of GPhA.

[9] Ibid.

[10] Although sometimes used interchangeably, *regulatory exclusivity* consists of two types: data exclusivity and marketing exclusivity. "*Data exclusivity* protects the safety and efficacy information—often termed the 'data package'—submitted by the brand-name firm from use by generic firms. As a result, a generic firm may not rely upon that data in support of its own application for FDA marketing approval for a period of years. Data exclusivity does not prevent a generic firm from submitting its own data package. In contrast, a *marketing exclusivity* prevents a competing firm from obtaining FDA approval whether or not it has generated its own safety and efficacy data.... The Hatch-Waxman Act allows generic firms to obtain a 180-day period of 'generic exclusivity' if they are the first to file an ANDA challenging a brand-name firm's patents. Generally speaking, this regulatory exclusivity precludes the FDA from approving another ANDA for the same product for the 180-day period." For further information, see CRS Report R42890, *The Role of Patents and Regulatory Exclusivities in Pharmaceutical Innovation*, by (name redacted).

[11] Andrew Hill, Dzintars Gotham, and Joseph Fortunak, et al., "Target prices for mass production of tyrosine kinase inhibitors for global cancer treatment," *BMJ Open*, vol. 6, no. 1 (January 27, 2016), pp. 1-10.

slightly lower than the brand-name manufacturer. However, the appearance of a second generic manufacturer reduces the average generic price to nearly half the brand name price. As additional generic manufacturers market the product, the prices continue to fall, but more slowly. For products that attract a large number of generic manufacturers, the average generic price falls to 20% of the branded price and lower."[12]

The 2016 GPhA report provides the following two illustrative examples.[13]

- Zocor (simvastatin) treats high cholesterol and reduces risk of heart attacks and related health problems. The brand price pre-patent expiry for this medicine was $2.62 per pill. The generic version currently sells for three cents per pill—a 99% savings. In 2015, more than 65 million prescriptions for this medicine were dispensed.
- Depression affects 19 million Americans across age, race and gender. Generic versions of the popular brand-name drug Zoloft became available in 2006. Last year [2015] there were 45 million prescriptions dispensed for generic versions of Zoloft (sertraline) at a price of six cents per pill. This is a 97% price reduction from the brand pre-expiry price of $2.18 per pill.

Recently media attention has focused on price increases for certain generic drugs. For example, between July 1, 2013, and June 30, 2014, the cost of the antibiotic tetracycline increased 17,714% and the heart drug digoxin increased 828%.[14] However, a review of the generic drug market by the Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation (ASPE), found that "about two-thirds of generic products appear to have experienced price declines in 2014." For the segments of the generic drug market that have experienced large price increases, ASPE provides the following explanations: "small markets with limited entry; the impact of mergers, acquisitions, and market exits; the ability to obtain new market exclusivities; and distribution activities."[15] ASPE states that "these problems apply to relatively small segments of the market and, while they lead to increased costs in certain therapeutic areas, they have little influence on overall spending increases."[16]

Funding for the premarket review of ANDAs submitted to FDA by generic drug sponsors is provided by direct appropriations from Congress and user fees paid by the generic drug industry. The following section of this report discusses the reauthorization by Congress of the Generic Drug User Fee Amendments of 2012 (GDUFA).

The Need for Generic Drug User Fees

FDA first gained the authority to collect user fees from the manufacturers of brand-name prescription drugs and biological products in 1992, when Congress passed the Prescription Drug

[12] FDA, CDER, "Generic Competition and Drug Prices," at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.

[13] The Generic Pharmaceutical Association, *2016 Generic Drug Savings & Access in the United States Report*, p. 8, at http://www.gphaonline.org/media/generic-drug-savings-2016/index.html.

[14] Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, *Understanding Recent Trends in Generic Drug Prices*, January 27, 2016, p. 6, at https://aspe.hhs.gov/pdf-report/understanding-recent-trends-generic-drug-prices.

[15] Ibid., p. 1.

[16] Ibid.

User Fee Act (PDUFA).[17] With PDUFA, FDA, industry, and Congress reached an agreement on two concepts:

1. performance goals—FDA would negotiate with industry on target completion times for various review processes; and
2. use of fees—the revenue from prescription drug user fees would be used for activities to support the review of new product applications and would supplement—rather than supplant—congressional appropriations to FDA.

The added resources from user fees allowed FDA to increase staff available to review applications and to reduce the median review time for standard applications. Over the years, Congress has added similar user fee authority regarding medical devices, animal drugs, and biosimilars.[18] User fees constitute 42% of the FY2016 FDA budget.[19]

According to FDA, the Hatch-Waxman Act led to "a significant regulatory challenge" for the agency. That is because FDA's resources did not keep pace with the increasing number of ANDAs and other submissions related to generic drugs.[20] This resulted in delayed approvals of generic drugs, "a major concern for the generics industry, FDA, consumers, and payers alike."[21] In March 2012, median review time for generic drug applications was approximately 31 months and FDA had a backlog of over 2,500 ANDAs.[22] At that time, FDA was receiving about 100 NDAs and 800-900 ANDAs each year.[23]

In addition, FDA had to conduct more inspections as the number of manufacturing facilities grew, "with the greatest increase coming from foreign facilities."[24] In March 2012, the number of foreign Finished Dosage Form (FDF) manufacturers exceeded the number found in the United States.[25] Moreover, the generic industry was experiencing "significant growth in India and China," a trend that was expected to continue.[26] According to FDA, foreign inspections "represent a significant challenge and require significant resources."[27] The agency's website states:

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[17] See CRS Report R42366, *Prescription Drug User Fee Act (PDUFA): 2012 Reauthorization as PDUFA V*, by (name redacted) and CRS Report RL33914, *The Prescription Drug User Fee Act: History Through the 2007 PDUFA IV Reauthorization*, by (name redacted)

[18] See CRS Report R44517, *The FDA Medical Device User Fee Program: MDUFA IV Reauthorization*, by (name redacted); CRS Report RL34459, *Animal Drug User Fee Programs*, by (name redacted); and CRS Report R44620, *Biologics and Biosimilars: Background and Key Issues*, by (name redacted).

[19] CRS Report R44576, *The Food and Drug Administration (FDA) Budget: Fact Sheet*, by (name redacted) and (name redacted)

[20] Statement of Janet Woodcock, M.D., Director, 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.

[21] Ibid.

[22] Ibid.

[23] Margaret A. Hamburg, FDA Commissioner, "Remarks at the GPhA Annual Meeting," February 18, 2011, http://www.fda.gov/NewsEvents/Speeches/ucm244201.htm.

[24] Woodcock, "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.

[25] Ibid. FDF means a drug product in the form in which it will be administered to a patient (e.g., a tablet, capsule, solution, or topical application). FFDCA Section 744A(6).

[26] Ibid.

[27] Ibid.

> Prior to GDUFA, FDA was required to inspect domestic human generic drug manufacturers every 2 years, but no such requirement existed for foreign manufacturers. This disparity between domestic and foreign manufacturing facilities, combined with insufficient resources, created significant vulnerabilities in the global prescription drug supply chain. Approximately 80% of active ingredients used in human generic medicines and marketed in the United States are manufactured in foreign countries, and more than half of finished products are manufactured overseas.[28]

Generic Drug User Fee Amendments (GDUFA I)

In order to expedite ANDA reviews and bring parity to domestic and foreign inspection schedules, FDA had proposed generic drug user fees in each annual budget request to Congress beginning with the FY2008 request.[29] Such fees became possible when the Food and Drug Administration Safety and Innovation Act (FDASIA, P.L. 112-144) became law in July 2012. Title III of FDASIA, the Generic Drug User Fee Amendments (GDUFA), authorized FDA to collect fees from industry for agency activities associated with generic drugs. Under what is now called GDUFA I, such fees are allowed to be collected from October 2012 through September 2017.

GDUFA I set the total amount of generic drug fees collected for FY2013 at $299 million.[30] It established the types of fees to be paid by the manufacturer. The first two fees listed below are paid at the time of filing or application submission; the facility fees are annual fees for each establishment:

- application fee for an ANDA,
- application fee for a prior approval supplement (PAS)[31] to an ANDA,
- Drug Master File[32] fee,
- facility fee for the facility making the API, and
- facility fee for the facility producing the FDF.

[28] FDA, GDUFA Performance Reports, at http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm384247.htm.

[29] The FY2008 budget request for FDA included proposed generic drug user fees in a table (http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/BudgetReports/2008FDABudgetSummary/ucm122804.htm) and in narrative ("Improving Generic Drug Review Performance," http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/BudgetReports/2008FDABudgetSummary/ucm122189.pdf.

[30] FFDCA Section 744B(b). GDUFA I included a provision that for FY2013, the first year under the agreement, $50 million of the $299 million collected would come from a one-time backlog fee to be paid by sponsors of generic drug applications that were pending at the time of enactment.

[31] A prior approval supplement (PAS) means a request from an ANDA holder to FDA to approve a change in the drug substance, drug product, production process, quality controls, equipment, or facilities covered by an approved ANDA when that change has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. FFDCA Section 744A(10). Final PAS guidance was released in October 2016: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM404441.pdf.

[32] "A Drug Master File (DMF) is a submission to FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs. The submission of a DMF is not required by law or FDA regulation. A DMF is submitted solely at the discretion of the holder. The information contained in the DMF may be used to support an Investigational New Drug Application (IND), an NDA, an ANDA, another DMF, an Export Application, or amendments and supplements to any of these." FDA, "Drug Master Files: Guidelines," September 1989, at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm122886.htm. See also 21 C.F.R. 314.420.

The law also specified the proportion that each type of fee contributes to the total collected and provided a methodology for the calculation of an annual inflation adjustment for the remaining four fiscal years under GDUFA I, FY2014 through FY2017.

Like PDUFA, the first GDUFA agreement included limitations, often referred to as triggers, designed to ensure that user fees supplement, rather than replace, congressional appropriations. The limitations require that budget authority (appropriations minus fees) go no lower than the FY2009 amounts, adjusted for inflation, for (1) FDA salaries and expenses overall and (2) human generic drug activities.

Again similar to PDUFA, but different from the narrower medical device (MDUFA) and biosimilar (BsUFA) definitions, GDUFA defined human generic drug activities to include the review of submissions and drug master files, approval letters and complete response letters, letters regarding deficiencies, inspections, monitoring or research, postmarket safety activities, and regulatory science.

Other provisions under the original GDUFA agreement include risk-based biennial inspections, parity of domestic and foreign inspection schedules by FY2017, a $15,000–$30,000 higher inspection fee for a foreign facility than for a domestic facility to reflect cost differences, streamlined hiring authority, and required annual performance and financial reports. The current FY2017 fee rates under GDUFA are shown in **Table 1**. The FDA provides information on the amount of GDUFA fees collected each fiscal year and how the fees are spent in the annual financial reports.[33] Annual performance reports provide data on FDA's progress in meeting GDUFA performance goals and commitments.[34]

Table 1. FY2017 Fee Rates Under GDUFA

Fee Category	Fee Rate for FY2017
Abbreviated New Drug Application (ANDA)	$70,480
Prior Approval Supplement (PAS) to an ANDA	35,240
Drug Master File (DMF)	51,140
Active Pharmaceutical Ingredient (API) Facility—Domestic	44,234
API Facility—Foreign	59,234
Finished Dosage Form (FDF) Facility—Domestic	258,646
FDF Facility—Foreign	273,646

Source: *Federal Register*, July 27, 2016.

Effect of GDUFA I on ANDA Backlog

Under GDUFA I, FDA committed to reviewing and taking regulatory action on 90% of the ANDA backlog by September 30, 2017. In July 2016, FDA announced that it had met this commitment more than a year ahead of schedule.[35] As of September 30, 2016, FDA had taken

[33] GDUFA Financial Reports are available at http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/GDUFA/default.htm.

[34] GDUFA Performance Reports are available at http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm384247.htm.

[35] "FDA Completes Review of GDUFA Backlog," PharmaTech.com, July 11, 2016, at http://www.pharmtech.com/fda-completes-review-gdufa-backlog.

action on 94% of ANDAs and 93% of PASs that were in the original backlog.[36] "When GDUFA I began on October 1, 2012, there were 2,866 pending ANDAs that were counted as the backlog."[37]

At an October 2016 GPhA conference, FDA Office of Generic Drugs (OGD) Director Kathleen Cook Uhl stated that "under GDUFA I, FDA has issued 2,273 approvals and tentative approvals as of September 30, 2016." [38] In addition, according to Ted Sherwood, director of OGD's Office of Regulatory Operations, the generic drug pipeline contains "approximately 2,200 applications pending at the agency" and "another roughly 1,800 are back with the sponsors due to either a complete response letter (1,500) or a tentative approval (300)."[39] A complete response letter (CRL) describes all of the deficiencies that FDA has identified in an ANDA that must be satisfactorily addressed before the ANDA can be evaluated for approval. According to FDA OGD Director Uhl, "these are not on the agency clock, we have no idea when they're coming back or if they're coming back to the FDA for another review cycle."[40]

If the ANDA submitted by the generic drug sponsor lacks "crucial information—about their research, when the original drug will lose patent protection, or relevant court cases," then the review process can slow down.[41] For example, according to an FDA official, "one applicant seeking to produce a drug for irritable bowel syndrome ignored the propensity of its inactive ingredient to cause diarrhea. Too many generic drug submissions showed a lack of knowledge about medicine or how to make it."[42] According to Kenneth Phelps, owner of Camargo Pharmaceutical Services, which develops generic drugs, "the dirty little secret of the generic industry is that they always submitted deficient [applications]."[43] As long as the FDA accepted the applications, companies would "submit and then add the right stuff later. Honestly, it was a game."[44]

FDA representatives at the October 2016 GPhA conference indicated that in total the agency has approved more than 16,000 ANDAs. "However, that number drops down to approximately 10,000 when you look at currently approved ANDAs that have not been withdrawn. Of the 10,000 currently approved ANDAs, more than 20% have been approved since GDUFA" was implemented but "many of those ANDAs don't even go to market.... Innovator drugs for which there are no approved competitors, but for which ANDAs are pending, account for less than 2% of all drugs."[45] Therefore, "if there's a lack of generic competition to branded products for off patent drugs, the answer may lie with industry" not with FDA.[46]

According to another source, "there are only 23 innovator drugs with ANDAs pending and no patent or exclusivity protection. That means there's only 23 ANDAs awaiting approval or a CRL and nothing else stopping the generic drug makers from bringing competition to the market

[36] Sue Sutter, "FDA Aims To 'Pierce The Rhetoric' On Generic Application Backlog," *Pink Sheet*, October 31, 2016.

[37] Ibid.

[38] Ibid.

[39] Ibid.

[40] Ibid.

[41] Sheila Kaplan, "One reason for high drug prices: a huge backlog of unapproved generic drugs," *STAT*, December 29, 2015, at https://www.statnews.com/2015/12/29/generic-drugs-backlog/.

[42] Ibid.

[43] Ibid.

[44] Ibid.

[45] Sue Sutter, "FDA Aims To 'Pierce The Rhetoric' On Generic Application Backlog," *Pink Sheet*, October 31, 2016.

[46] Ibid.

except for FDA. But there are another 125 innovator drugs with no approved generics and no ANDAs submitted."[47]

The FDA website states that 651 ANDAs were approved in FY2016, 492 ANDAs were approved in FY2015, and 409 ANDAs were approved in FY2014.[48]

Reauthorization (GDUFA II)

As is the case with several other FDA user fee authorities,[49] the five-year generic drug user fee authority is scheduled to sunset on September 30, 2017. The reauthorization process is outlined in the FFDCA as amended by GDUFA.[50] The process began on June 15, 2015, when FDA held a public meeting on the reauthorization of the GDUFA program.[51] Beginning in October 2015 through August 2016, the agency held negotiation sessions with the generic drug industry on the reauthorization agreement; minutes of these meetings are posted on the FDA website.[52] In addition, the law directs FDA to hold monthly discussions with representatives of patient and consumer advocacy groups; minutes of these stakeholder meetings are also found on the FDA website.[53]

In October 2016, the agency posted on its website the draft GDUFA agreement—GDUFA II—setting FDA performance goals and procedures for FY2018 through FY2022.[54] Another public meeting was held on October 21, 2016.[55] Following a 30-day comment period (open through November 16, 2016), a final GDUFA II recommendation will be submitted to Congress by January 15, 2017.

GDUFA II Fees

FDA and industry agreed that under GDUFA II user fees should total $493.6 million annually, adjusted each year for inflation, in order to maintain current productivity and implement proposed

[47] Zachary Brennan, "Generic Drug Backlog at FDA: A Dive Into the Confusing Numbers," *RF Regulatory Focus*, November 1, 2016, at http://raps.org/Regulatory-Focus/News/2016/11/01/26106/Generic-Drug-Backlog-at-FDA-A-Dive-Into-the-Confusing-Numbers/.

[48] FY2016 data at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm375079.htm; FY2015 data at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm473746.htm; FY2014 data at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm427830.htm.

[49] Prescription drug (PDUFA), medical device (MDUFA) and biosimilar (BsUFA).

[50] FFDCA Section 744C(d).

[51] FDA, GDUFA Reauthorization Public Meetings, at http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm444958.htm.

[52] FDA, GDUFA Reauthorization Negotiation Sessions, at http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm256662.htm.

[53] FDA, GDUFA Reauthorization Stakeholder Meetings, at http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm466008.htm.

[54] FDA, *GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022*, at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf, and *GDUFA II Fee Structure Summary*, at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525236.pdf.

FDA, GDUFA Reauthorization Public Meetings, at http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm444958.htm.

[55] Ibid.

GDUFA II improvements.[56] According to FDA, ANDA reviews are the primary workload driver of the GDUFA program.[57] Under GDUFA I, the agency projected that it would receive approximately 750 ANDAs per year and planned and budgeted according to that projection.[58] However, FDA actually received approximately 1,000 ANDAs per year.[59] To address the increased workload, FDA hired additional staff and is projected to spend about $430 million in user fee funds in the fifth year of GDUFA I.

GDUFA II Goals

Under the GDUFA II performance goal agreement between FDA and industry, the agency will review and act on 90% of standard original ANDAs within 10 months of the date of ANDA submission.[60] This continues the goal that GDUFA I set for the year 5 cohort in FY2017, the final year of the GDUFA I agreement. By way of comparison, under GDUFA I the goal was for FDA to review and act on 60% of ANDAs within 15 months of submission date for the year 3 cohort, and 75% of original ANDA submissions within 15 months of submission date for the year 4 cohort.[61]

Similarly, GDUFA II will continue another goal from the final year of GDUFA I (FY2017): FDA will review and act on 90% of standard PASs within 6 months of the date of PAS submission if preapproval inspection is not required and within 10 months of the date of PAS submission if preapproval inspection is required.[62] Under GDUFA I, for PASs not requiring inspection, the goal was for FDA to review and act on 60% of PASs within six months from the date of submission for receipts in FY2015 and 75% of PASs within six months from the date of submission for receipts in FY2016.[63] For PASs requiring inspection, the goal under GDUFA I was for FDA to review and act on each of the three cohorts within 10 months.

GDUFA II is adding two new features: a priority ANDA and a priority PAS. FDA will review and act on 90% of priority ANDAs within eight months of the date of ANDA submission, if the sponsor has submitted a complete and accurate facilities data package, called a Pre-Facility Communication (PFC), two months prior to the date of ANDA submission.[64] For the priority PAS, FDA will review and act on 90% of priority PASs within four months of the date of PAS submission if preapproval inspection is not required.[65] If preapproval inspection is required, FDA

[56] See GDUFA Meeting Presentation Slide #60 at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM526282.pdf.

[57] Ibid.

[58] Ibid.

[59] FDA received 1,103 ANDAs in FY2012, 968 ANDAs in FY2014, 1,473 in FY2015; see Slide #19 at http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM487832.pdf.

[60] FDA, *GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022*, p. 4 at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.

[61] FDA, "Generic Drug User Fee Act Program Performance Goals and Procedures," p. 9, at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf.

[62] FDA, *GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022*, p. 6 at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.

[63] FDA, "Generic Drug User Fee Act Program Performance Goals and Procedures," p. 12, at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf.

[64] FDA, *GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022*, p. 4 at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.

[65] FDA, *GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022*, p. 6 at http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.

will review and act on 90% of priority PASs within eight months of the date of PAS submission, provided the applicant submits a complete and accurate PFC two months prior to the date of PAS submission.[66]

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[66] Ibid.