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Economic Impacts of the Generic Drug User Fee Act Fee Structure

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ABSTRACT

Background: A Food and Drug Administration (FDA) Generic Drug User system, Generic Drug User Fee Amendment of 2012 (GDUFA), started October 1, 2012, and has been in place for over 3 years. There is controversy about the GDUFA fee structure but no analysis of GDUFA data that we could find. **Objective:** To look at the economic impact of the GDUFA fee structure. **Methods:** We compared the structure of GDUFA with that of other FDA Human Drug User fees. We then, using FDA-published information, analyzed where GDUFA facility and Drug Master File fees are coming from. We used the Orange Book to identify the sponsors of all approved Abbreviated New Drug Applications (ANDAs) and the S&P Capital IQ database to find the ultimate parent companies of sponsors of approved ANDAs. **Results:** The key differences between the previous structure for Human Drug User fees and the GDUFA are as follows: GDUFA has no approved product fee and no first-time or small business fee exemptions and GDUFA charges facility fees from the time of filing and charges a foreign facility levy. Most GDUFA fees are paid by or on behalf of foreign entities. The top 10 companies hold nearly 50% of all approved ANDAs but pay about 14% of GDUFA facility fees. **Conclusions:** We conclude that the regressive nature of the GDUFA fee structure penalizes small, new, and foreign firms while benefiting the large established firms. A progressive fee structure in line with other human drug user fees is needed to ensure a healthy generic drug industry.

Keywords: generic drug, Generic Drug User Fee Act (GDUFA), fee structure, pharmaceuticals.

Introduction

The modern US generic drug industry was created by passage of the Price Competition & Patent Term Restoration Act (Hatch-Waxman Act), signed into law on September 24, 1984. This act established a mechanism for generic drug approval, the Abbreviated New Drug Application (ANDA) [1]. An ANDA relied on an existing, marketed product (the Referenced Listed Drug [RLD]) for evidence of safety and efficacy and on bioequivalence to the RLD as evidence that the generic product was "equivalent" to the RLD [1].

Among other things, Hatch-Waxman Act directed that the Food and Drug Administration (FDA) review ANDAs within 180 days of receipt. Another requirement is that the FDA determine the appropriate demonstration of bioequivalence for RLDs for which systemic blood levels measured following single doses in healthy volunteers are not an appropriate measure of therapeutic equivalence [1]. Products manufactured under approved ANDAs are required to be manufactured in compliance with current Good Manufacturing Practices, as are all FDA-regulated medical products.

At the inception of the ANDA, the FDA expressed concern that it would not be able to meet the 180-day review mandate the Act required. Although the FDA testified to the Congress that it could not meet the mandated review cycle, it reorganized and managed to meet the 180-day review cycle almost from the start [1]. As a result of meeting the mandate, the issue of resources to perform ANDA review faded from public view and FDA's ANDA review performance was judged satisfactory for 20 years following the passage of the Hatch-Waxman Act (excluding a period associated with the Generic Drug Scandal) [2,3].

The arrival of user fees for the services of the FDA was late in comparison with many other government departments [4]. There was a concern that the FDA was responsible for enforcing standards on industry to ensure safety and compliance. For this reason, establishing significant user fees was seen as a conflict of interest, in that industry would be essentially paying the salary of those charged with overseeing and enforcing standards on the industry. However, despite the potential for conflict of interest, user fees were established for New Drug Applications (and Biological License Applications) in 1992 [5]. These fees became collectively known as the Prescription Drug User Fee Act (PDUFA).

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The reason that the industry agreed so readily to Prescription Drug User Fee Act (PDUFA) was the implementation of new timelines in which to complete New Drug Application (NDA) reviews. Revenue from NDA products depends on the length of time before generics get onto the market, so any additional time on the market while the product is still protected from generic competition is very valuable. Money raised via PDUFA was spent primarily on additional staff to enable agreed NDA review times of 12 months or 6 months to be met by the FDA. The FDA performance against PDUFA-set targets has been very good and the brand industry continues to strongly support PDUFA [5].

The generic industry vigorously opposed the imposition of generic drug user fees when these were first proposed in 1992. Industry argued that generic drugs saved federal government health care programs billions of dollars and the cost of generic drug review was a tiny fraction of the savings. Opposition continued until 2009 when the major generic industry trade associations abruptly reversed their long-held position, and came out in favor of user fees. The major issue that changed the generic industry view on user fees was the same as that which encouraged the brand industry to embrace user fees—review cycle time. For most of the time since the Hatch-Waxman Act, the FDA had met or nearly met the 180-day mandate for review, so little would be gained in review turnaround by paying user fees as Figure 1 shows (original ANDAs received and pending by year figure compiled by the authors, available in Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.05.003). Most generic products cannot be approved until patent(s) or exclusivities or both protecting the RLD expire, so the generic company approval target is first generic market formation and not the brand target of "as quickly as possible." Although bioequivalence methodology is a minor issue compared with review cycle time [6], it is becoming more important because some of the products in this category have large market values and are more attractive targets for generic drug companies. Another issue concerns FDA Compliance Inspection of foreign facilities that develop and manufacture generic drugs for import into the United States. The proportion of generic drugs being developed and manufactured in other countries has been increasing [7]. It has long been held by US domestic manufacturers that FDA Compliance Inspections of foreign firms were not as thorough as those conducted for domestic firms [8]. In addition, the FDA has been falling behind on its Inspectional Program for foreign facility inspections [9]. The FDA has ascribed this situation to lack of resources, and generic drug user fees would allow more resources to provide equal inspectional intensity and timing for all facilities and so maintain a "level playing field."

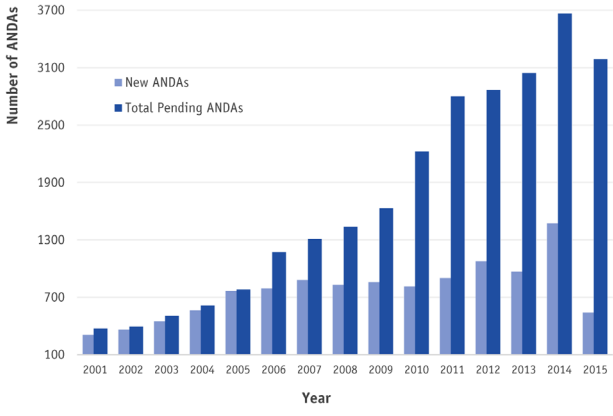

Fig. 1 – Original ANDAs received & pending by year. *Source:* **Pre-GDUFA data source: Karst [35,36]. Post-GDUFA data source: U.S. Food and Drug Administration [37].**

Methods

We compared the fee structure of GDUFA with that of other FDA Human Drug User fee acts including PDUFA, the Medical Device User Fee Act, and the Biosimilar User Fee Act. Descriptions of these structures are available on the FDA Web site or accessible through the FDA Web site.

We used FDA-published self-identified facility database that includes all finished dose form (FDF) manufacturers and active pharmaceutical ingredient (API) manufacturing facilities that are referenced in at least one pending or approved ANDA. We used the lists for fiscal year 2013, 2014, and 2015, identified the location of each facility by country, and then used this information to analyze how GDUFA facility fees are geographically distributed. We used the FDA-published "Available for Reference" list of Drug Master Files (DMFs) to identify the sponsors of all DMFs and the location of each sponsor by country to analyze how GDUFA DMF fees are geographically distributed.

We then used the FDA-published Orange Book database to find the sponsor of all approved ANDAs and the S&P Capital IQ database to find the ultimate parent companies of sponsors of approved ANDAs. We then analyzed how the approved ANDAs are distributed among different pharmaceutical companies and constructed the top 10 companies list by ANDAs owned.

Results

How the Fee Structure of GDUFA Differs from that of Other Human Drug User Fee Acts?

PDUFA fee structure

The first FDA user fee system was the PDUFA system, which has three parts: a fee for NDA (and supplement) filing, an annual facility fee, and an annual marketed product fee [10]. Each part is intended to raise approximately the same amount of revenue. In addition, PDUFA allows a "first-time" exemption from paying application fees for small companies [11]. The user fees are levied in exchange for FDA performance goals. The important goal is application review time, 12 months for "standard" NDAs and 6 months for "priority" NDAs. The FDA must report to the Congress annually on PDUFA performance goals. Congress also established a "sunset" provision for PDUFA, requiring reauthorization of user fees every 5 years.

PDUFA user fees are structured in such a way that they levy the highest annual fees on the largest firms with the highest number of approved NDAs. Once a firm has at least one approved NDA, the firm pays an annual facility fee, and on average larger firms have more facilities than do small ones who have only one facility (an explicit analysis about top NDA holders is provided in Appendix 2 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.05.003), so they pay a higher proportion of facility fees in total. Each approved NDA pays an annual product fee; again, the largest firms have the most approved NDAs and they pay a higher proportion of these fees. In addition, with the one-time user fee exemption, only firms actually participating in the brand drug marketplace pay user fees. PDUFA has a progressive user fee structure as a firm's total fees paid—the sum of application, establishment, and product fees paid by firms—are directly related to the number of applications, establishments, and products, and so to the firm's level of market participation.

GDUFA fee structure

The concept of a generic drug user fee, primarily directed at funding resources for review and compliance activities, was first publicly discussed during 2010. Supporting groups included the