RESEARCH ARTICLE

The Impact of Generic Drug User Fee Act on Generic Drug Export from India

Rajender Singh[1,2], Swati Singh[1], Anil Kumar[2], GT Kulkarni[3*], Arti Thakkar[1*]

[1]*Department of Regulatory Affairs, Amity Institute of Pharmacy, Amity University Uttar Pradesh, Noida, Uttar Pradesh, India*
[2]*Regulatory Affairs Division, Mankind Research Centre, IMT Manesar, Gurugram, Haryana, India*
[3]*Department of Pharmaceutics, Gokaraju Rangaraju College of Pharmacy, Hyderabad, India*

Received: 18th October, 2022; Revised: 13th November, 2022; Accepted: 28th November, 2022; Available Online: 25th December, 2022

ABSTRACT

Generic drugs are drugs that have a similar active ingredient, dosage type, strength, and route of administration as a brand name medication. India is the hub of generic drugs and exports to various countries. The regulations for generics have been evolving through the years for better control of the price and quality of generic drugs. In this study, we have formulated a questionnaire consisting of questions on review time, communication with authority, the quality of products, and future expectations of the industry. Most people agreed that there had been a change since the introduction of generic drug user fee act (GDUFA). It has helped in reducing the review time of backlog applications, quick review for new applications, and raised certain expectations from the industry for the future of GDUFA. Communication has also improved between the industry and the food and drug administration (FDA), which has helped the applicant better understand the expectation of the authority.

Keywords: Generic Drug User Fee Act, Generic drugs, United States Food and Drug Administration (USFDA), Abbreviated new drug application.

International Journal of Pharmaceutical Quality Assurance (2022); DOI: 10.25258/ijpqa.13.4.20

How to cite this article: Singh R, Singh S, Kumar A, Kulkarni GT, Thakkar A. The Impact of GDUFS on Generic Drug Export from India. International Journal of Pharmaceutical Quality Assurance. 2022;13(4):470-474.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The generic industry vigorously opposed the implementation of generic drug user fees when it was proposed in 1992.[1] As per the industry, generic drugs helped federal government healthcare programs save billions of dollars, and the cost of generic drug review was just a tiny fraction of the savings. The generic industry continued to oppose the implementation of generic drug user fees until 2009. At this point, the abbreviated new drug application (ANDA) review cycle times started increasing significantly. This led the generic industry to rethink its long-held position, and the major generic industry trade associations favored user fees.[2]

In 2009, after realizing the importance of generic drugs, which were providing therapeutically equivalent medicines but at a lesser cost, the food and drug administration (FDA) decided to cut down the time for review of generic drug applications. This was intended to make generic drugs available to consumers in a short period without compromising quality and efficacy. To bring more and more generic drugs into the market in a short time through an effective review process, the FDA introduced the generic drug user fee program to get appropriate funding for resource management to ensure that consumers continue to receive the substantial benefits that are given by the generic drug.[3,4]

The generic drug user fee act (GDUFA) is designed to speed access to safe and effective generic drugs for the public and reduce costs to the industry. Appropriate steps are taken according to the FDA to approve applications that abide by the guidance. The purpose of GDUFA is to help the FDA ensure that participants of the US generic drug system comply with US quality standards and that the patient can get medicines at a nominal cost.[5,6]

The GDUFA program was designed to keep the individual fee amounts as low as possible to ensure that consumers receive significant benefits offered by the generic drugs. The expenses of bringing a product into the market have declined after the user fees were adopted, resulting in reduced costs of drugs. The American public received health benefits due to the GDUFA program along with these generic companies, and specifically, the first-time entrants got some additional benefits.[7] No user fee program existed for generic drugs before 2012 when legislation was passed. User fees are renegotiated with the industry every 5 years and must be reauthorized by congress and signed into law by the president.

Since the passage of GDUFA, user fees have played a critical role in expediting the generic drug review and approval processes. Currently, GDUFA III is running since October 1, 2022. Before this, two user fee agreements related to generic

**Author for Correspondence: artirthakkar@gmail.com*

drugs have completed their terms in the United States, GDUFA I and II, which have transformed the research landscape to support the development of generic drug products. GDUFA I (2012-2017) enabled an increase in FDA-supported research related to generic drug products. It allowed companies to get their products approved at a faster pace and reach the patient safely. GDUFA II (2018-2022) began on October 1, 2017, and was applicable through September 2022. GDUFA II added a significant new aspect to the generic drug development process in the form of pre-abbreviated new drug application (ANDA) meetings with the FDA. These pre-ANDA meetings helped companies to discuss new or alternative development strategies for complex generic drug products.[8-10] GDUFA II continued the public meetings, and the annual list of priorities added additional opportunities for generic drug industry input into research priorities and added additional reporting of research outcomes.[11]

Further, in the present study, we have gathered feedback through questionnaires of regulatory experts on various aspects of the submission process post-GDUFA. This questionnaire has been framed keeping in mind that India is a big generic hub, from where at least 40% of drugs are exported to the US market. Opinions of people from the generic industry have been collected with the help of this questionnaire and feedback evaluated to understand how the submission and review process has been impacted by the introduction of these laws.

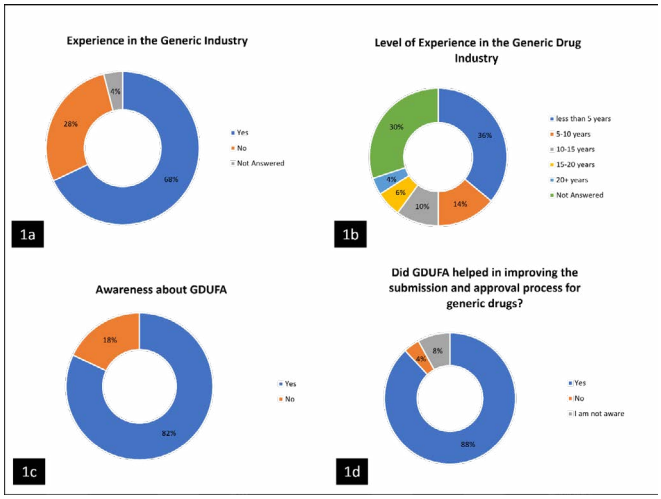

Figure 1: Experience of the participants, level of experience, and awareness about GDUFA. Figure 1 describes feedback on questions 1 to 5 which includes the experience of the participants in the generic industry (Figure 1a); level of experience of the participants (Figure 1b); awareness about the GDUFA (Figure 1c); impact of GDUFA on submission/approval process (Figure 1d).

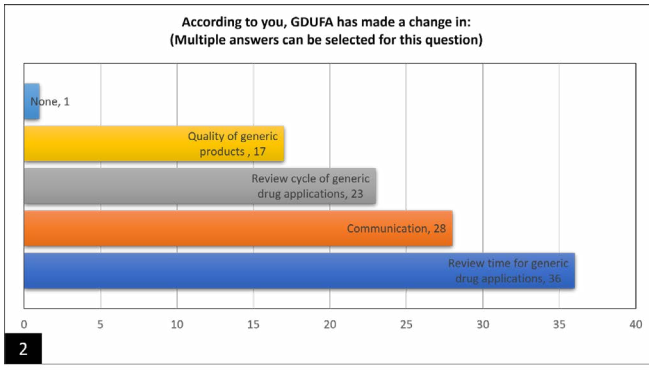

Figure 2: Overall changes occurred due to GDUFA.

METHOD

We surveyed to collect information on some of the important aspects concerning GDUFA. The questions based on communication with the FDA, the timeline for approval, review cycle time, quality of products, and any further expectations of the industry from the future reauthorizations of GDUFA were covered. Communication with FDA; has it become any easier to ask questions before sending the application to the agency, timely approval of the applications, reduce the amount of time taken for the review of the application and any further improvements expected by the industry with regards to GDUFA have been evaluated in this survey. The survey was sent to 70 people, out of which 50 responded. The survey was shared as a link: (https://docs.google.com/forms/d/e/1FAIpQLSdU_RR0WaLXs0lFcVlVHm6MHVGSyO-fzXWlTPjoEbbFDXPd5Q/viewform?vc=0&c=0&w=1&flr=0&usp=mail_form_link) of the questionnaire to collect the views from the pharmaceutical industry. All the questions are depicted in Table 1. The data collected has then been converted to a graphical presentation for easy understanding.

RESULTS AND DISCUSSION

We framed the questions covering important aspects like communication, the timeline for approval, the review cycle, the quality of products, and any further expectations of the industry from the future reauthorizations of GDUFA have been covered. All the feedback was converted in terms of graphs and discussed hereby. Figure 1 describes feedback on questions 1 to 5, which includes the experience of the participants in the generic industry (Figure 1a); the level of experience of the participants (Figure 1b); awareness about the GDUFA (Figure 1c); the impact of GDUFA on submission/approval process (Figure 1d) and changes occurred due to GDUFA (Figure 2).

It is clear from Figure 1 that about 68% of the participants were aware of the generic industry (Figure 1a) and about 36% had about 5 years of experience, 14% had 5–10 years, and there were about 10% of participants with 10–15 years of experience (Figure 1b). Out of all participants, about 82% were aware of the GDUFA (Figure 1c), and 88% believed that GDUFA helped in the improvement of the submissions and approval process (Figure 1d).

About 36 participants believe that GDUFA has changed the review time for generic drug applications. However, 28 deem GDUFA has impacted communication, 23 believe review cycle of generic drug applications, whereas 17 believe GDUFA influenced the quality of the product, as depicted in Figure 2.

Communication and Timeline for Approval and Review

Figure 3 describes the overall impact on communication and review post-GDUFA. Opinion on any changes after GDUFA

Table 1: Questions of the Questionnaire

S. No.	*Questions*
1	Experience of the person in the generic industry
2	Experience level in the generic drug industry
3	General awareness about GDUFA
4	Feedback if GDUFA implementation helped improve the submission and approval process for generic drugs
5	Impact of GDUFA implementation
Communication and timeline for approval and review	
6	Has GDUFA implementation improved communication for ANDA submissions
7	Has GDUFA implementation improved the review time of ANDAs
8	Any delays experienced by the firm in ANDA approval
9	Any possibility of a reduction in review cycles
Review Cycle	
10	Has GDUFA implementation improved effectiveness and transparency in the ANDA review process
Quality of the Product	
11	Has GDUFA implementation made any positive impact on the quality of drug products
12	Has GDUFA implementation made any positive impact on inspection and compliance
13	Any concerns related to compliance inspection
14	Effectiveness of the PFC process for priority review and ANDA approval
15	Are the amounts of GDUFA program fees justified?
16	Will a separate GDUFA website be more convenient?
17	Assessment of priority assignment under GDUFA III based on given options

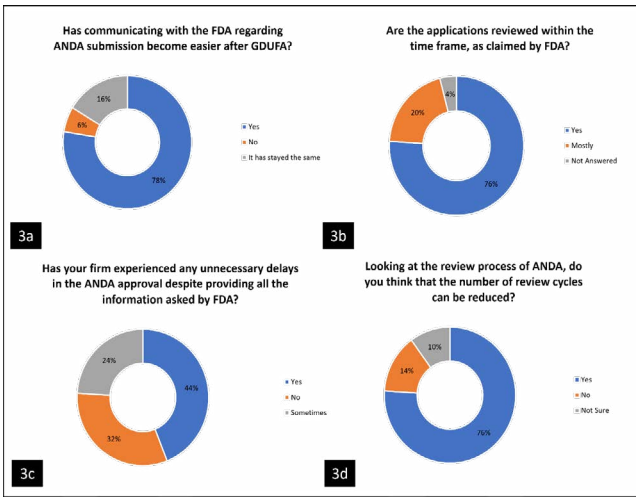

Figure 3: The overall impact on communication and review post-GDUFA Opinion on any changes after GDUFA implementation is given in Figure 3a. Review time is within the timeframe as claimed by FDA described in Figure 3b. An experience by the applicant of having an unnecessary delay in ANDA approval is given in Figure 3c. Opinion on a reduced number of the review cycle is described in Figure 3d.

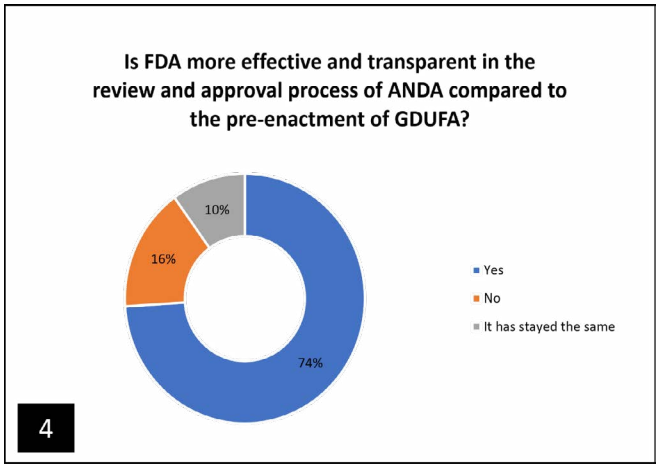

Figure 4: Opinion on FDA's effective and transparent working post-GDUFA.

implementation is given in Figure 3a. Review time is within the timeframe as claimed by FDA described in Figure 3b. An experience by the applicant of having an unnecessary delay in ANDA approval is given in Figure 3c. Opinion on a reduced number of the review cycle is described in Figure 3d.

Almost 78% of participants confirmed that the submission process is easier post-GDUFA (Figure 3a). About 76% believe applications are reviewed within the timeframe; however, 20% do not agree with that (Figure 3b). About 44% faced unnecessary delays in approval, whereas 32% did not face any delay (Figure 3c). Nearly 76% of participants mentioned that the number of review cycles could be reduced (Figure 3d).

Review Cycle

Opinion on FDA's effective and transparent working post-GDUFA is given in Figure 4. Almost 74% believe that the FDA's review and approval process of ANDA is now more effective and transparent compared pre-enactment of GDUFA.

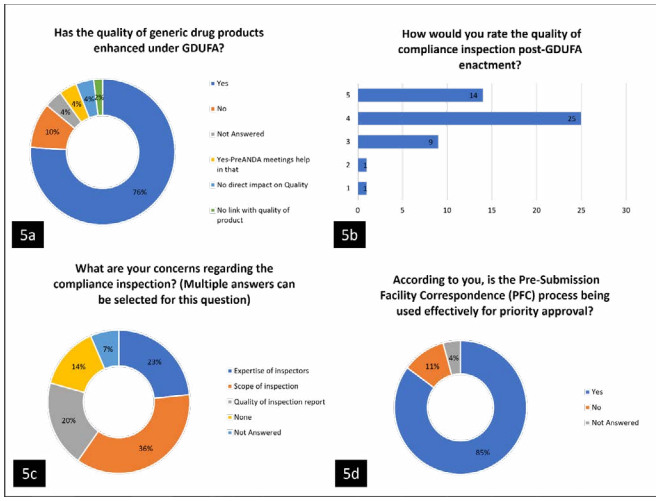

Figure 5: Impact of GDUFA on the quality of the product.Opinion on quality enhanced under GDUFA is described in Figure 5a. The impact of GDUFA on the quality of compliance inspection is discussed in Figure 5b. Concerns of the participants regarding compliance inspection are given in Figure 5c. The opinion of participants regarding the Pre-Submission Facility Correspondence (PFC) process used for priority ANDA review and approval is given in Figure 5d.

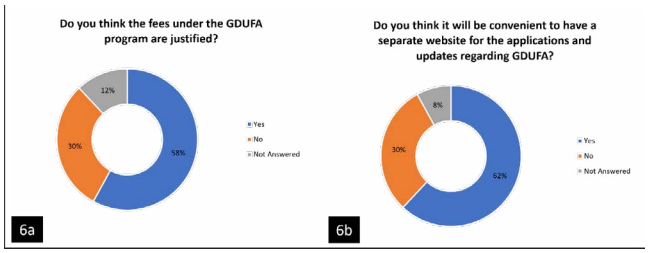

Figure 6: Participants' opinions about the fees and separate websites for applications and updates regarding the GDUFA.Participants' opinion about the fees post-GDUFA is given in Figure 6a. Opinion on having a separate website for generic applications and updates regarding GDUFA is described in Figure 6b.

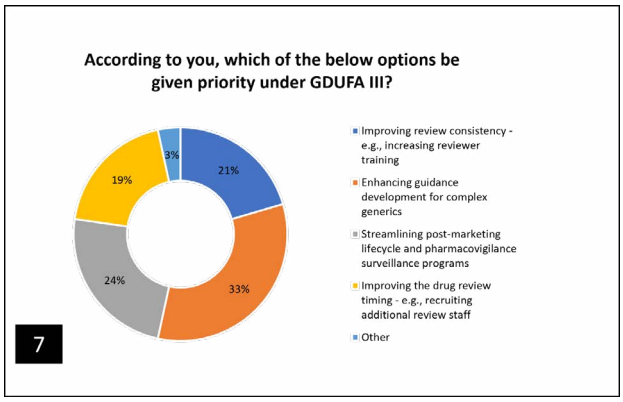

Figure 7: Parameters to be considered as a priority under GDUFA III.

Quality of the Product

Opinion on quality enhanced under GDUFA is described in Figure 5a. The impact of GDUFA on the quality of compliance inspection is discussed in Figure 5b. Concerns of the participants regarding compliance inspection are given in Figure 5c. The opinion of participants regarding the pre-submission facility correspondence (PFC) process used for priority approval is given in Figure 5d.

About 80% of the participant's opinion that the product's quality has been enhanced under GDUFA, as depicted in Figure 5a. Participants were asked to give a rating from 1-5 (1-poor; 2-unsatisfactory; 3-satisfactory, 4-very satisfactory, and 5-outstanding) for compliance inspections, and about 50% rated 4 (very satisfactory) and 28% rated 5 (outstanding) as described in Figure 5b. About 36% of participants had concerns about the scope of the inspection, and 23% had concerns about the expertise of the inspection. About 20% were concerned about the quality of inspection, as described in Figure 5c. Almost 85% of participants confirm that PFC process is being used effectively for priority approval, as illustrated in Figure 5d.

Participants' opinion about the fees post-GDUFA is given in Figure 6a. Opinion on having a separate website for generic drug applications and updates regarding GDUFA is described in Figure 6b. Different options, such as being given priority under GDUFA III, were asked, and data was collected as described in Figure 7.

About 58% believe that fees under the GDUFA program are justified, whereas the remaining doesn't agree, as represented in Figure 6a. About 62% believe that it will be more convenient if there is a separate website for the generic drug applications and updates regarding GDUFA, and the rest do not agree with the statement, as illustrated in Figure 6b. About 33% of participants believe that priority should be given to enhancing guidance development for complex generics, whereas 24% of participants deem that priority should be given to streamlining post-marketing lifecycle and pharmacovigilance surveillance programs and about 21% consider that improving review consistency must be given priority, however, 19% thinks priority must be given in improving drug review timing as illustrated in Figure 7.

The survey conducted contains views and opinions of people from the generic industry with an experience range of fewer than 5 to 10 years, and most of them were aware of GDUFA. The inference drawn from the survey is that GDUFA has brought an improvement in the submission and approval process of ANDAs for generic drugs. Generic drug applicants feel that there has been a major improvement in the review timeline for applications, followed by improvement in communication, review cycle, and quality of products. More than 80% of people favored submission to the USFDA, which is more effective and transparent in the ANDA review and approval process compared to the period before GDUFA enactment.

In terms of inspection, 80% of people indicated that the quality of inspections is very good (4-rating), along with a concern for the scope of inspections, and 60% of people feel that PFC is being used more effectively for priority review and approval. Looking at future expectations, people are hoping to see an improvement in review consistency, enhancing guidance

development for complex products, and streamlining post-market lifecycle and pharmacovigilance.

The questionnaire feedback suggests that the GDUFA has introduced changes in review time to reduce the backlogs. This change has helped the industry to file more applications and get timely approval for their products. Timely approval, hence, helps in releasing the product in the market and providing cost-effective and quality products to the patient. Along with reduced review time, communication and transparency have also been improved. FDA is more transparent in the review process, and their initiative of 'pre-ANDA meetings' has helped in better communication between the applicant and the agency.

Thus, GDUFA came at a decisive time since the public health achievement of generic medicines had caused a significant challenge. Due to inadequate resources, the FDA needed to be able to maintain pace with a rising number of ANDAs submitted for review. Approximately 4,000 generic drug applications were pending. Nonetheless, GDUFA gave the FDA the required resources and personnel to eliminate the backlog and brought generic drugs to the market and patients more promptly.[12]

CONCLUSION

India is the hub of generic drugs and exports to various countries. The United States imports a good number of generics from India and more than 90% of the prescriptions are filled with generic drugs. The regulations for generics have been evolving through the years for better control of the competition of price and quality of generic drugs. The survey suggested that GDUFA has brought an improvement in the submission and approval process for generic drugs. People feel that there has been a major improvement in the review time of applications, followed by improvement in communication, review cycle, and quality of products as indicated in the data above. A total of 80% of the participants were in favor of the FDA being more effective and transparent in the ANDA review and approval process compared to the time before GDUFA enactment.

The overall conclusion is that the GDUFA has introduced changes in review time for reducing backlogs. This change has helped the industry file more applications and get timely approval for their products.

ACKNOWLEDGMENT

The authors are thankful to Amity University, Uttar Pradesh and Mankind Pharma Ltd. for providing basic infrastructure to carry out the present study. The authors are very thankful to Mr. Mahesh Kumar, Senior Office Assistant, Amity Institute of Pharmacy, Amity University Uttar Pradesh, for helping in the preparation of all the illustrations.

CONFLICT OF INTEREST

There is no conflict of interest between the authors.

FUNDING

This article received no specific grant from any funding agency in the public, commercial or not-to-profit sectors. It is a self-sponsored work.

REFERENCES

1. Hutt PB. The Regulation of Drug Products by the US Food and Drug Administration. In The Textbook of Pharmaceutical Medicine (eds Griffin JP, Posner J and Barker JR). Edn 7. John Wiley & Sons, Ltd. New York, USA, 2013, 461-500.
2. Venkatesh MP, Sukumaran TS. GDUFA: Implementation and the Latest Amendments. International Journal of Current Pharmaceutical Review and Research. 2018; 9(5):77-81. Available from: http://impactfactor.org/PDF/IJCPR/9/IJCPR,Vol9,Issue5,Article4.pdf
3. Lionberger RA. Innovation for Generic Drugs: Science and Research Under the Generic Drug User Fee Amendments of 2012. Clinical Pharmacology & Therapeutics. 2019; 105(4):878-885. Available from: https://doi.org/10.1002/cpt.1364
4. Food and Drug Administration Safety and Innovation Act (FDASIA. US Food & Drug Administration. 2018. Available from: www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-administration-safety-and-innovation-act-fdasia.
5. Singh R, Singh S, Kumar A, Kulkarni GT, Thakkar AR. Impact of generic drug user fee act and other initiatives on generic drug approval process in the USA. Asian Journal of Pharmaceutical Research and Health Care. 2022; 14(1):7-15. Available from: https://doi.org/10.4103/ajprhc.ajprhc_7_21
6. LoCastro S. Impact of GDUFA II Fee Structure on Generic Drug Change Evaluation. West Pharmaceutical Services, Inc. 2017. https://www.westpharma.com/-/media/westpharma/files/regulatory-support/impact-of-gdufa-ii-on-generic-drug-change-evaluation.ashx
7. CDER. What is GDUFA? Overview of the Generic Drug User Fee Amendments of 2012 (GDUFA). FDA Publication. 2022. https://www.accessdata.fda.gov/cder/GDUFA_overview/topic7/topic7/da_01_07_0010.htm
8. FDA. GDUFA Performance Reports. 2022a. https://www.fda.gov/about-fda/user-fee-performance-reports/gdufa-performance-reports
9. FDA. PDUFA Performance Reports. 2022b. https://www.fda.gov/about-fda/user-fee-performance-reports/pdufa-performance-reports
10. Picurro JA. GDUFA II: Do You Have a Strategy ? FDA Watch, Contract Pharma. 2018:1-15. https://www.contractpharma.com/issues/2018-05-01/view_fda-watch/gdufa-ii-do-you-have-a-strategy
11. GDUFA Performance Reports. US Food & Drug Administration. 2020. https://www.fda.gov/about-fda/user-fee-performance-reports/gdufa-perforance-reports
12. Blank C. GAO: Generic drug approvals are too slow. Formulary Watch, 2019. https://www.formularywatch.com/view/gao-generic-drug-approvals-too-slow