Self-Identification of Generic Drug Facilities, Sites, and Organizations

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

September 2016
Generics

Self-Identification of Generic Drug Facilities, Sites, and Organizations

Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm
7519 Standish Place, Rockville, MD 20855
Phone: 240-276-9300
http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
September 2016
Generics

TABLE OF CONTENTS

Contains Nonbinding Recommendations

Self-Identification of Generic Drug Facilities, Sites, and Organizations
Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended to assist human generic drug facilities, sites, and organizations by describing how to comply with the self-identification requirement contained in the Generic Drug User Fee Amendments of 2012 (Public Law 112-144, Title III), commonly referred to as GDUFA.

Under GDUFA, human generic drug facilities, sites, and organizations are required to submit identification information electronically to FDA annually. FDA is issuing this guidance to help human generic drug facilities, sites, and organizations meet the self-identification requirement. Topics discussed in this guidance include:

- which types of generic facilities, sites, and organizations are required to self-identify;
- what information is requested;
- what technical standards are to be used for electronically submitting the requested information; and
- the penalty for failing to self-identify.

This guidance also explains generally which types of generic facilities, sites, and organizations will be required to pay user fees.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

II. BACKGROUND

On July 9, 2012, GDUFA was signed into law by the President.[2] GDUFA is designed to speed the delivery of safe and effective generic drugs to the public and reduce costs to industry. GDUFA enables FDA to assess user fees to support critical and measurable enhancements to FDA's generic drugs program. GDUFA will also significantly improve global supply chain transparency by requiring owners of facilities producing generic drug products, active pharmaceutical ingredients (API), and certain other sites and organizations that support the manufacture or approval of these products to electronically self-identify with FDA and update that information annually.

Self-identification is required for two purposes. First, it is necessary to determine the universe of facilities required to pay user fees. Second, self-identification is a central component of an effort to promote global supply chain transparency. The information provided through self-identification enables quick, accurate, and reliable surveillance of generic drugs and facilitates inspections and compliance.

Most facilities that self-identify are required to pay an annual facility user fee. These include facilities manufacturing, or intending to manufacture, API of human generic drugs and/or finished dosage form (FDF) human generic drugs. Other sites and organizations must self-identify, but are not required to pay the annual facility user fee. These include facilities that solely manufacture positron emission tomography (PET) drugs, or sites and organizations that only perform testing, repackaging, or relabeling operations. Please note that while repackagers are not required to pay user fees, packagers are, in most cases, FDF manufacturers and subject to facility fees.

A separate system for the electronic self-identification of generic industry facilities, sites, and organizations was established for GDUFA. Entities required to register and list (under section 510 of the Federal Food, Drug, and Cosmetic Act or section 351 of the Public Health Service Act), and those required to self-identify under GDUFA submit information separately to the respective systems. Each system populates its own database to meet unique requirements and deadlines. The separate GDUFA system uses the same platform and technical standards already familiar to manufacturers required to register and list.

III. GDUFA SELF-IDENTIFICATION REQUIREMENTS

The following discussion explains who is required to self-identify, what information is required for submission, and what the process is for submitting self-identification information.

[2] On October 5, 2012 the President signed into law the FDA User Fee Correction Act of 2012. This act amends GDUFA so that due dates for GDUFA user fees in fiscal year 2013 are not dependent on enactment of an appropriations act.

A. Who Is Required to Self-Identify?

The following types of generic industry facilities, sites, and organizations are required to self-identify with FDA:

1. Facilities[3] that manufacture, or intend to manufacture, human generic drug APIs or FDFs, or both.[4]

2. Facilities that package the FDF of a human generic drug into the primary container/closure system and label the primary container/closure system.[5]

3. Sites that are identified in a generic drug submission and pursuant to a contract with the applicant remove the drug from a primary container/closure system and subdivide the contents into a different primary container/closure system.

---

[3] GDUFA has defined the term "facility" to identify those businesses required to pay fees and for self-identification. GDUFA defines a facility as a business or other entity under one management, either direct or indirect, at one geographic location or address, engaged in manufacturing or processing an API or an FDF. It does not include a business or other entity whose only manufacturing or processing activities are one or more of the following: repackaging, relabeling, or testing. Separate buildings within close proximity are considered to be at one geographic location or address if the activities in them are closely related to the same business enterprise; are under the supervision of the same local management; and are capable of being inspected by FDA during a single inspection. GDUFA further states that if a business entity would meet the definition of a facility but for being under multiple management, the business or entity is deemed to constitute multiple facilities, one per management entity.

[4] For purposes of self-identification and payment of fees, GDUFA defines API and FDF manufacturers differently from the way these categories of manufacturers have been defined historically. For example, generic drug manufacturers who mix an API when the substance is unstable or cannot be transported on its own are considered API manufacturers and not FDF manufacturers for self-identification and the payment of GDUFA fees only.

GDUFA defines an FDF as:
(A) a drug product in the form in which it will be administered to a patient, such as a tablet, capsule, solution, or topical application;
(B) a drug product in a form in which reconstitution is necessary prior to administration to a patient, such as oral suspensions or lyophilized powders; or
(C) any combination of an active pharmaceutical ingredient (as defined in the statute) with another component of a drug product for purposes of production of a drug product described in subparagraph (A) or (B).

GDUFA defines an API as:
(A) a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended—
(i) to be used as a component of a drug; and
(ii) to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or
(B) a substance intended for final crystallization, purification, or salt formation, or any combination of those activities, to become a substance or mixture described in subparagraph (A).

[5] Facilities that package the FDF of a human generic drug into the primary container/closure system and label the primary container/closure system are considered to be manufacturers, whether or not that packaging is done pursuant to a contract or by the applicant itself.

4. Bioequivalence (BE)/bioavailability (BA) sites that are identified in a generic drug submission and conduct clinical BE/BA testing, bioanalytical testing of samples collected from clinical BE/BA testing, and/or in vitro BE testing.

5. Sites that are identified in a generic drug submission and perform testing of one or more attributes or characteristics of the FDF or the API pursuant to a contract with the applicant to satisfy a current good manufacturing practice (CGMP) testing requirement (excludes sites that are testing for research purposes only).

B. What Information Is Required for Submission?

The following information is required to meet the self-identification requirement in GDUFA:

1. D-U-N-S Numbers

FDA requires Data Universal Numbering System (D-U-N-S) numbers for both the facility or site and the registrant owner of the facility or site if the facility or site is in a different location than the registrant owner location. A D-U-N-S number is required to uniquely identify the registrant (the owner or operator) and each physical location of the business's facility or site (e.g., branches, divisions, and headquarters).

A D-U-N-S number is a unique nine-digit sequence provided by Dun & Bradstreet. The D-U-N-S number is specific for each site. Each distinct physical location of an entity (e.g., branch, division, and headquarter) would be assigned a different D-U-N-S number.

The site-specific D-U-N-S number is a widely recognized business identification tool and serves as a useful resource for FDA in identifying and verifying certain business information submitted by a user.

If no D-U-N-S number has been assigned, a business entity may obtain one at no cost directly from Dun & Bradstreet. A new number may be obtained, or an existing number verified, by phone or online. Existing facilities D-U-N-S numbers may also be verified on FDA's current registration site for drug establishments.[6]

> *Note*: It takes Dun & Bradstreet approximately 30 business days to process a new D-U-N-S number and communicate it via email. A business entity may receive a D-U-N-S number in approximately 10 business days for an expedited service fee. Please note that a business entity may not request or apply for a new D-U-N-S number on behalf of another business entity due to the verification procedures used by Dun & Bradstreet.

More information is available at the Dun & Bradstreet web page. See also the step-by-step instructions for obtaining a D-U-N-S number for businesses based either in the United States or abroad.

[6] http://www.accessdata.fda.gov/scripts/cder/drls/default.cfm

2. Facility Establishment Identifier

Facilities must also submit a Facility Establishment Identifier (FEI), a unique identifier designated by FDA to assign, monitor, and track inspections of regulated firms. [7]
A business entity that has previously obtained an FEI number may verify its FEI number by sending an email request to FDAGDUFAFEIRequest@fda.hhs.gov.

Alternatively, business entities that have not previously registered with FDA can obtain an FEI number by sending an email request to FDAGDUFAFEIRequest@fda.hhs.gov. Please type "GDUFA FEI Request" in the subject line and include the following information in the body of the email:

Firm Name
Facility Address including City, Province, Country, and Mail Code
Size of Firm
Type of Operation (Manufacturer, Lab, etc.)
Type of Industry: Drugs

Requests for issuance of FEI numbers associated with GDUFA self-identification are typically processed within 10 to 15 business days.

3. Additional Information

FDA requests the name and contact information for the registrant owner and facility information, including name, type of business operation, and contact information. Submitters are also asked to indicate whether they manufacture drugs that are not generic drugs.

C. What Is the Process for Submitting Self-Identification Information?

The self-identification process is similar to other FDA electronic submission standards. Self-identification files should be formatted in the same electronic messaging standard used for drug registration and listing information and for the content of labeling for abbreviated new drug applications (ANDAs). This standard, known as Health Level Seven Structured Product Labeling (SPL), allows information to be exchanged, searched, and combined with other data sources in a manner that supports health information technology initiatives to improve patient care.

Providing Regulatory Submissions in Electronic Format — Drug Establishment Registration and Drug Listing[8] provides detailed instructions on how to submit information using SPL. FDA also offers tools and information for creating and submitting SPL files. Additional information can be found at www.fda.gov/edrls.

[7] For the Agency's policy on the assignment of FEIs, please refer to Field Management Directive (FMD) #130, *Official Establishment Inventory (OEI) Development and Maintenance*, which provides standardized definitions and associated procedures to facilitate consistency of data in the OEI.
[8] http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072339.pdf

D. What Is the Penalty for Failing to Self-Identify?

Although GDUFA provides no explicit penalty for sites and organizations that fail to comply with the self-identification requirement, the failure of a site or organization to comply with the law and self-identify may raise significant concerns about that site. Such failure is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because sites fail to comply with self-identification requirements.

More importantly, under GDUFA, if a facility fails to self-identify, all FDF or API products manufactured at the facility and all FDFs containing APIs manufactured at the facility will be deemed misbranded.[9] It is a violation of federal law to ship misbranded products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of the misbranded products. Products that are deemed misbranded because of failure of the facility to self-identify are subject to being denied entry into the United States.

[9] 21 U.S.C. §352(aa)