



Generic Drug User Fee Amendment
(GDUFA II)

SPL Industry Technical Specification
Information

Electronic Self-Identification of
Generic Drug Facilities or Sites

Date: August 2017

Background

FDA is establishing databases, systems, and processes that help generic drug companies perform electronic self-identification of facilities and sites involved in the development and manufacturing of generic drugs. Electronic self-identification is required by all such facilities and sites, whether or not user fees payments are required, if the facilities and sites are identified or intended to be identified in an approved or pending generic drug submission. Those that are required to self-identify, whether or not their facilities and sites are located within the United States territories and possessions, include:

- (A) Active Pharmaceutical Ingredients (API) Facilities;
- (B) Finished Dosage Forms (FDF) Facilities;
- (C) Positron Emission Tomography (PET) Facilities;
- (D) Clinical Bioequivalence (BE) or Bioavailability (BA) Study Sites;
- (E) In Vitro Bioequivalence Testing or Bioanalytical Sites;
- (F) Contract API/FDF Analytical Testing Sites;
- (G) Contract Packaging Sites; or
- (H) Contract Repackaging Sites

A more detailed description of these operations and their respective Business Operation codes appears later in the document. Additionally, those who are required to self-identify must specify whether they are also a facility or site that manufacturers non-generic drugs.

The Self-identification process will employ the same electronic submission method and format as electronic Drug Registration and Listing (eDRLS). Generic facilities mentioned above, or whoever is sending in the submission on their behalf, will need to obtain a WebTrader account with the FDA's Electronic Submissions Gateway (ESG). If the company already has a WebTrader account, a second is not necessary. Information about obtaining a WebTrader account may be found at the FDA's ESG website, <http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm>.

GDUFA Self-identification submissions will utilize Extendable Markup Language (XML) file formats which conform to Health Level Seven (HL-7) message exchange standards for Structured Product Labeling (SPL), versions 4 and 5. Specific data elements for the GDUFA Self-identification submissions are described below.

Self-identification will not replace the ESG or eDRLS processes; these processes will continue as they currently exist. Similar to eDRLS processes, self-identifiers can generate electronic SPL files using commercial tools, FDA's eSubmitter tool, or FDA's SPL Xforms and submit their SPL files through the FDA's ESG. The technical details for utilizing SPL files are available in the SPL Implementation Guide located on the FDA Data Standards Council Web site, <http://www.fda.gov/oc/datacouncil/spl.html>.

Although various types of information are needed to facilitate electronic self-identification, Data Universal Numbering System (DUNS) numbers will be used by FDA to identify registrants as well as facilities and sites. Obtaining a DUNS number can take 20 to 40 business days

through a basic service provided at no cost or through an expedited service for a nominal fee. The process for obtaining DUNS numbers is available through FDA's Business Entity Identifiers page located at:

<http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm162544.htm>

Once the appropriate DUNS numbers are obtained, three types of information are needed to create an SPL file that will enable completion of the electronic self-identification process. To ensure quality data collection and management, entities will provide document information, registrant information, and facility information for each generic drug facility and site that is required to self-identify.

SPL Data Element Descriptions

1. Document Information: The document information is used for tracking the SPL files and includes the Type of Document, ID Root, Set ID Root, Version Number, and Effective Time.

1.1. Type of Document: Select "Generic Drug Facility Identification Submission."

1.2. ID Root: The ID Root uniquely identifies a specific SPL file. Each new version of an SPL file has a new ID root.

1.3. Set ID Root: The Set ID Root uniquely identifies a group of versions of an SPL file

1.4. Version number: The version number provides an order for different versions of an SPL file. The version number is a whole number greater than zero. The version number is increased with each change. Enter a number in the version number field.

1.5. Effective Time: The effective time provides a date reference to the SPL version. The date includes the year, month, and date using the format YYYYMMDD, and must be in the current year to be accepted by the FDA. Enter the date for the SPL file.

2. Registrant Information: The registrant is the owner or operator of the facility or site. The information includes registrant name and registrant DUNS number.

2.1. Name: Enter the headquarters' business name of the registrant that is self-identifying a facility or site.

2.2. Registrant DUNS Number: Each registrant has its own unique site-specific DUNS number. The registrant DUNS number will be utilized by FDA to identify ownership of each facility or site. Enter the registrant DUNS number without hyphens for the company headquarters.

2.3. Registrant Contact: The registrant contact is the person FDA contacts about the registration information. The contact information includes the name, address, contact telephone number, and email address.

2.3.1. Name: Enter the name of the registrant.

2.3.2. Mailing Address: Enter the street name and number of the mailing address for the registrant.

2.3.2.1. Street: Enter the street name and number of the mailing address for the registrant.

2.3.2.2. City: Enter the city of the mailing address for the registrant.

2.3.2.3. State: Enter the state of the mailing address of the registrant. If in the United States, enter the two letter state abbreviation. If there is no state, as with certain addresses outside the United States, leave the field empty.

2.3.2.4. Country: Enter the three character country code using the ISO 3166-1 standard for the mailing address of the registrant.

2.3.2.5. Postal Code: Enter the postal code of the mailing address of the registrant. If there is no postal code, as with certain addresses outside the United States, leave the field empty.

2.3.3. Telephone Number: Enter one contact telephone number for the registrant. Telephone numbers are global telephone numbers using the Uniform Resource Identifier (URI) for Telephone Numbers RFC 3966 (no letters; begin with “+”; include hyphens to separate the country code, area codes and subscriber number; extensions are separated by “;ext=”).

2.3.4. Email Address: Enter one primary business email address for the registrant.

3. Facility Information: The Facility Information includes Facility Name, Facility DUNS number, FDA Establishment Identifier (FEI), Business Operation, and Contact Information.

3.1. Name: Enter the name of the facility or site to be self-identified.

3.2. Facility DUNS Number: Each business location (e.g., headquarters, branch, subsidiary, establishment, importer, US agent) has its own unique site-specific DUNS number. The Facility DUNS numbers will be utilized by FDA as a key identifier for linking the self-identification of facilities and sites to their user fee payments. Enter the facility or site DUNS number without hyphens.

3.3. FEI: FDA assigns an FDA establishment identifier (FEI) after the initial registration for tracking inspections. Enter the FEI number of the establishment.

3.4. Physical Address: Enter the street name and number of the physical address of the establishment.

3.4.1. Street: Enter the street name and number of the physical address of the establishment

3.4.2. City: Enter the city of the physical address of the establishment.

3.4.3. State: Enter the state of the physical address of the establishment. If in the United States, enter the two letter state abbreviation. If there is no state, as with certain addresses outside the United States, leave the field empty.

3.4.4. Country: Enter the three character country code using the ISO 3166-1 standard of the physical address of the establishment.

3.4.5. Postal code: Enter the postal code of the physical address of the establishment. If there is no postal code, as with certain addresses outside the United States, leave the field empty.

3.5. Business Operations: From the choices below or from the table following, select all of the following types of business operations performed at each facility or site.

3.5.1. Active Pharmaceutical Ingredients Manufacture (API) Facilities: Select option “API Manufacture” if the facility or site manufactures:

(A) Substance, or a mixture when the substance is unstable or cannot be transported on its own, intended to be used as a component of a drug and intended 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) Substance intended for final crystallization, purification, or salt formation or any combination of those activities, to become the final active pharmaceutical ingredient as defined in paragraph (A) above.

3.5.2. Finished Dosage Forms Manufacture (FDF) Facilities: Select option “FDF Manufacture” if the facility or site manufactures:

(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) 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 with another component of a drug product for purposes of production of such a drug product as defined in paragraphs (A) or (B) above.

Entities that package drugs, other than those defined as repackagers (see below), are considered FDF manufacturers.

3.5.3. Positron Emission Tomography Drug Production (PET) Facilities: Select option “Positron Emission Tomography Site Drug Production” if the facility or site manufactures radioactive drugs administered to patients, which allow cameras and/or scanners to take images of internal body organs and tissues. This includes a positron emission tomography drug or active pharmaceutical ingredient for a positron emission tomography drug, which:

- (A) Exhibits spontaneous disintegration of unstable nuclei by the emission of positrons and is used for the purpose of providing dual photon positron emission tomographic diagnostic images; and
- (B) Includes any nonradioactive reagent, reagent kit, ingredient, nuclide generator, accelerator, target material, electronic synthesizer, or other apparatus or computer program to be used in the preparation of such a drug.

3.5.4. Clinical Bioequivalence or Bioavailability Study (BE) or (BA) Study Sites: This option corresponds with the statutory category “clinical research organizations.” Select “Clinical Bioequivalence or Bioavailability Study” if the facility or site is a Clinical Research Organization (CRO) or is associated with a bioequivalence/bioavailability study and engages in activities that include administering investigative drugs to human subjects for the purpose of demonstrating bioequivalence to a Reference Listed Drug. Associated activities include, but are not limited to, screening subjects, administering drugs to subjects, collection of biological specimens (e.g. plasma, serum, or urine) and safety monitoring, as specified in the study protocol.

3.5.5. In Vitro Bioequivalence or Bioanalytical Testing Sites: This option corresponds with the statutory category “a site in which a bioanalytical study is conducted.” Select “In Vitro Bioequivalence or Bioanalytical Testing”, if the facility or site conducts in vitro bioequivalence testing or measures concentrations of drug, drug metabolite, or other analytes as specified in the study protocol, in specimens collected during in vivo bioequivalence/bioavailability trials.

3.5.6. Active Pharmaceutical Ingredients / Finished Dosage Forms Manufacture Analytical Testing Sites (Contract API/FDF Analytical Testing): Select option “API/FDF Analytical Testing” if the contract analytical testing facility or site is separate from the location of the processing facility for the API or the FDF and that is identified in the generic drug submission.

(A) Includes analytical testing sites that are responsible for testing one or more attributes or characteristics of the API including tests to verify purity, levels of impurities, particle size, and stability or;

(B) Includes analytical testing sites that are responsible for testing one or more attributes or characteristics of the FDF, including testing FDF in-process material, testing to qualify components used in the FDF, and testing to qualify components used in the FDF, and testing the stability of the FDF.

3.5.7. Contract Packaging Sites (Pack): Select option “Pack” if the contract facility or site is separate from the location of the processing facility for the API or FDF and the site is owned or operated and identified in a generic drug submission, which include only packager sites that are named in an ANDA application. The facility or site is responsible for packaging the FDF into the primary container/closure system and/or labeling the primary container/closure system.

(A) Includes such activities as taking tablets from a large drum of tablets and packaging the tablets into individual bottles for retail sale and/or pharmacy use.

3.5.8. Contract Repackaging Sites (Repack): Select option “Repack” if the contract facility or site is separate from the location of the processing facility for the API or FDF and the site is identified in a generic drug submission. The facility or site is responsible for removing the drug from a primary container/closure system and placing the contents into a different primary container/closure system.

(A) Includes facilities that remove a drug from a primary container/closure system and subdivide the contents into a different primary container/closure system (i.e., takes tablets out of a plastic bottle and packages the tablets into blister packaging).

3.6. Business Operations Qualifier: The Business Operations Qualifier is used in conjunction with the Business Operations types to indicate the facility or site also manufactures non-generic drugs. For each business operation type that is selected, **also** specify whether the facility or site also manufactures non-generic drugs.

3.6.1. Manufactures Non-Generics: Select option “Manufactures Non-Generics” business operations qualifier if the facility or site also manufactures non-generic drugs. For example, a facility or site that selects a business operation for API would use the business operations qualifier to specify whether they are also a facility or site that manufactures non-generic drugs, and so on for each business operation that applies.

3.6.2 Contract Manufacturing: Select this option if the contract facility is manufacturing of a part or all of final dosage form (FDF) and the contract facility is not identified in an approved ANDA owned by that facility or its affiliates. A contract facility or site may perform one or more FDF manufacturing operations and activities or may engage an outside party or parties to perform some or all of the FDF operations and activities under contract.

3.7. Facility Contact: The facility contact is the person FDA contacts regarding the establishment. The contact information includes the name, address, contact telephone number, and email address.

3.7.1. Name: Enter the name of the facility contact person.

3.7.2. Mailing address: Enter the street name and number of the mailing address of the facility contact person.

3.7.2.1. Street: Enter the street name and number of the mailing address of the facility contact person

3.7.2.2. City: Enter the city of the mailing address of the facility contact person.

3.7.2.3. State: Enter the state of the mailing address of the facility contact person. If in the United States, enter the two letter state abbreviation. If there is no state, as with certain addresses outside the United States, leave the field empty.

3.7.2.4. Country: Enter the three character country code using the ISO 3166-1 standard of the mailing address of the facility contact person.

3.7.2.5. Postal code: Enter the postal code of the mailing address of the facility contact person. If there is no postal code, as with certain addresses outside the United States, leave the field empty.

3.7.3. Telephone number: Enter one contact telephone number for the facility contact person. Telephone numbers are global telephone numbers using the Uniform Resource Identifier (URI) for Telephone Numbers RFC 3966 (no letters; begin with "+"; include hyphens to separate the country code, area codes and subscriber number; extensions are separated by ";ext=").

3.7.4. Email Address: Enter one email address for the facility contact person.

Business Operations cross-walk to current FDA, SPL acceptable terms

SPL NCI Concept Code	SPL Business Operation Type	FDA Facility/Site Type	Short Description
C82401	API Manufacture	Active Pharmaceutical Ingredients (API) Facility or Site	A facility or site identified or intended to be identified in an approved or pending generic drug submission, which manufactures an Active Pharmaceutical Ingredient (API).
C101510	FDF Manufacture	Finished Dosage Forms (FDF) Facility or Site	A facility or site identified or intended to be identified in an approved or pending generic drug submission, which manufactures a finished dosage form (FDF). Entities that package drugs, other than those defined as repackagers are considered FDF manufacturers.
C91403	Positron Emission Tomography Drug Production	Positron Emission Tomography (PET) Facility or Site	A facility or site identified or intended to be identified in an approved or pending generic drug submission, which manufactures Positron Emission Tomography (PET) drugs solely or in addition to other drugs.

SPL NCI Concept Code	SPL Business Operation Type	FDA Facility/Site Type	Short Description
C101512	In Vitro Bioequivalence or Bioanalytical Testing	In Vitro Bioequivalence Testing or Bioanalytical Facility or Site	This option corresponds with the statutory category “a site in which a bioanalytical study is conducted.” A facility or site that conducts in vitro bioequivalence testing or measures concentrations of drug, drug metabolite, or other analyses as specified in the study protocol, in specimens collected during in vivo bioequivalence/ bioavailability trials.
C101509	API/FDF Analytical Testing	Contract API/FDF Analytical Testing Facility or Site	A contract analytical testing facility or site that is separate from the location of the processing facility for the API or the FDF and that is identified in the generic drug submission.
C84731	Pack	Contract Packaging Facility or Site	A contract packaging facility or site identified in a generic drug submission.
C73606	Repack	Contract Repackaging Facility or Site	A contract repackaging facility or site identified in a generic drug submission.

SPL NCI Concept Code	SPL Business Operation Type	FDA Facility/Site Type	Short Description
C101886	Manufactures Non-Generics	Business Operations Qualifier	A qualifier that specifies, for each business operation type declared, whether it is also a facility or site that manufactures non-generic drugs.
C132491	Contract Manufacturing	Business Operations Qualifier	Manufacturing of a part or all of final dosage form (FDF) that take place in a contract facility and the contract facility is not identified in an approved ANDA owned by that facility or its affiliates

Additional Help

In addition to the links mentioned above, please note the following helpdesk email accounts which may be of assistance in preparing and sending GDUFA Self-identification submissions:

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| esgprep@fda.hhs.gov | - creating a WebTrader account |
| esgreg@gnsi.com | - technical assistance with production WebTrader accounts |
| CDEReFacility@fda.hhs.gov | - technical assistance with SPL files related to CDER |
| spl@fda.hhs.gov | - technical assistance with SPL files related to CBER |
| AskGDUFA@fda.hhs.gov | - General questions, assistance, and policy issues with Self-identification and other GDUFA related initiatives |