

Electronic Drug Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance**

**December 2016
Compounding and Related Documents**

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<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

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I. INTRODUCTION

This guidance explains how facilities that elect to register with FDA as outsourcing facilities are to submit drug product reports, consistent with section 503B of the Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b).¹ Section 503B of the FD&C Act provides that a facility that elects to register with FDA as an outsourcing facility must report to FDA certain information about the drugs compounded at that outsourcing facility in the form and manner that FDA may “prescribe by regulation or guidance.”² This guidance describes who must report and what information they must provide and explains that drug compounding reports must be submitted in structured product labeling (SPL) format using FDA’s electronic submissions system.

Because Congress gave FDA explicit statutory authority to establish binding requirements in guidance as to the form and manner in which reports are to be prepared, those portions of this guidance relating to such form and manner are not subject to the usual restrictions in FDA’s good guidance practices (GGP) regulations (i.e., the requirements that guidances not establish legally enforceable responsibilities and that guidances prominently display a statement of the document’s nonbinding effect).³

II. BACKGROUND

The DQSA added new section 503B to the FD&C Act. Under section 503B(b), a compounder can elect to become an outsourcing facility by registering with FDA and meeting the other requirements described in section 503B of the FD&C Act.⁴ Outsourcing facilities are inspected by FDA on a risk-based schedule and must comply with other provisions of the FD&C Act, such as current good manufacturing practice (CGMP) requirements. Details on other requirements applicable to outsourcing facilities are the subject of separate guidance documents.⁵ A facility that elects to become an outsourcing facility must, at the time of initial registration and twice each year, in June and December, submit to FDA a report identifying the drugs

¹ Section 503B was added to the FD&C Act by the Drug Quality and Security Act (DQSA), Pub. Law No. 113-54, on November 27, 2013.

² See section 503B(b)(2)(B).

³ See 21 CFR 10.115(d) & (i).

⁴ See the guidance for industry *Registration for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act*.

⁵ All FDA guidances are available on the FDA guidance web page. FDA updates guidances regularly. To make sure you have the most recent version of a guidance, always consult the guidance web page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

compounded by the facility during the previous six-month period.⁶ For each identified drug, the outsourcing facility must provide certain information, which is listed in section 503B(b)(2)(A)(ii).

III. SCOPE OF THIS GUIDANCE

This guidance addresses the provisions in the DQSA regarding the drug reporting requirements for registered outsourcing facilities. Separate guidance documents provide instructions on which facilities should register with FDA as outsourcing facilities and how to do so. FDA has modified its electronic submission system to accept the electronic reports for drugs compounded by registered outsourcing facilities in SPL format. This guidance provides instructions for outsourcing facilities to report compounded drugs in SPL format using FDA's electronic submission system, and supersedes FDA's draft guidance, *Interim Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act*.

IV. SUBMITTING COMPOUNDED PRODUCT REPORTS

A. Who Must Report and What Must They Report

Upon initial registration as an outsourcing facility under section 503B and twice each year (in June and December), each registrant must submit a drug product report to FDA.⁷ This means that even if the outsourcing facility has not compounded any drug products during the previous six-month period, it must submit a report to FDA indicating that it has not compounded any drug products during the period.

This report must identify all sterile and non-sterile drugs compounded at the outsourcing facility during the previous six-month period and provide all of the following information for each compounded drug⁸:

- The active ingredient and strength of active ingredient per unit
- The source of the active ingredient
- The National Drug Code (NDC) number of the source drug or bulk active ingredient, if available
- The dosage form and route of administration
- The package description
- The number of individual units produced
- The NDC number of the final product, if assigned⁹

For purposes of drug product reporting under section 503B(b), the *strength of the active ingredient per unit* is the strength of the active ingredient per dose of the product.

⁶ Section 503B(b)(2) of the FD&C Act.

⁷ Section 503B(b)(2)(A) of the FD&C Act.

⁸ Section 503B(b)(2)(A) of the FD&C Act.

⁹ Section 503B(b)(2)(A)(ii) of the FD&C Act.

The *NDC number* for both the source drug or bulk active ingredient and any finished drug product to which an NDC has been assigned must be submitted in the standard format of ten numerical digits with dashes separating the three segments, for example, in a 5-4-1, 5-3-2, or 4-4-2 configuration.

The *package description* refers to the description of the smallest individual saleable package of the product for distribution and must include the type of package (e.g., vial, syringe, bottle) and the volume per package (e.g., 100 ml vial, 5 ml syringe, 100 tablets per bottle).

The *number of individual units produced* refers to the number of the smallest individual saleable packages of product for distribution. For example, if a registered outsourcing facility compounds one thousand 100 ml vials of 5 mg/ml of Drug X, the *strength of the active ingredient per unit* is “5 mg/ml,” the *package description* is “100 ml vials,” and the *number of individual units produced* is “1,000 vials.” Similarly, if a registered outsourcing facility compounds 5 mg tablets of Drug Y in one thousand bottles of 100 tablets each, the *strength of the active ingredient per unit* is “5 mg,” the *package description* is “bottles of 100 tablets,” and the *number of individual units produced* is “1,000 bottles.”

B. When to Report

Registered outsourcing facilities must submit a report upon initial registration under section 503B of the FD&C Act and twice each year thereafter, once in June and once in December.¹⁰ Initial drug product reports must identify products compounded during the previous six month period, not including the month in which the facility registers. Semiannual drug product reports submitted between June 1 and June 30 of each year must report products produced during the previous six month period from December 1 through May 31. Semiannual reports submitted between December 1 and December 31 of each year must report drug products compounded during the previous six month period from June 1 through November 30.¹¹

C. How to Report

Section 503B(b)(3) of the FD&C Act requires outsourcing facilities to submit drug reporting information by electronic means, unless FDA grants a request for a waiver of such requirement “because use of electronic means is not reasonable for the person requesting the waiver.” FDA has modified its electronic submission system to accept electronic submissions in SPL format for drugs compounded by registered outsourcing facilities. Therefore, a facility that elects to register with FDA as an outsourcing facility must submit drug product reporting information using FDA’s electronic reporting system and the SPL format, unless FDA has granted the facility a waiver.

FDA has created a new SPL document type category for outsourcing facilities’ drug product report submissions. Outsourcing facilities making electronic submissions must submit drug

¹¹ Section 503B(b)(2)(A) of the FD&C Act.

product reporting information using the document type “Human Compounded Drug Label.”¹² Section IV of the guidance for industry *Providing Regulatory Submissions in Electronic Format — Drug Establishment Registration and Drug Listing* 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.

Although each compounded product could be reported in a separate SPL submission, techniques can be used to simplify and combine the submissions for products with identical active ingredients, different packaging presentations, formulations, and/or strengths. Multiple strengths, package sizes, and source NDC numbers can be reflected in a single SPL submission, which will reduce the number of SPL submissions that a facility will need to submit to FDA. For example, the following table contains data that could be consolidated into a single product SPL submission:

NDC of Final Product, If Assigned (Use FDA 10 digit format with hyphens)	Active Ingredient(s) (Enter each ingredient on a separate line directly beneath)	Strength of Active Ingredient in Final Product	Source NDC for Active Ingredient (Separate multiple source NDCs for the same active ingredient with a semicolon ";")	Dosage Form	Route of Administration	Package description	Number of units produced between 12/1/14 and 5/31/15 (integers only)
12345-678-90	Hydrocortisone	10%	23456-789-90	Cream	Topical	20oz jar	1000
12345-679-91	Hydrocortisone	5%	34567-8901-2	Cream	Topical	40oz jar	1500
12345-679-92	Hydrocortisone	5%	34567-8901-2	Cream	Topical	20oz jar	1200

Furthermore, SPL submissions can be saved, updated, and resubmitted for subsequent reporting periods instead of creating a new submission each time. In addition, any product that is not compounded in a particular 6 month period does not require an SPL submission, even if the outsourcing facility sent in a submission for that product previously.

Whether the product report is for initial registration or the semiannual reporting period, if an outsourcing facility has not compounded any products for the previous six month period, a report explicitly stating so must be submitted.¹³ This can be accomplished by creating a single Human Drug Compounded Drug Label SPL file and indicating “No Products to Report” in the data elements section.

FDA does not anticipate many instances in which electronic submission of reporting information will not be reasonable for a facility because the electronic system for submitting the information is an internet-based system accessible to all facilities seeking to register. It is likely to be easier

¹² The SPL document type name “Human Compounded Drug Label” was chosen by the FDA Data Standards Council to distinguish drug product reporting submissions under section 503B from drug registration and listing submissions under section 510.

¹³ Section 503B(b)(2)(A).

to report product information electronically than in paper form. However, to apply for a waiver from the requirement to electronically submit drug reporting information, please provide a written request with a complete explanation of why the use of electronic means is not reasonable to the following:

Drug Registration and Listing System Staff
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

or

Email: edrls@fda.hhs.gov

If you are granted a waiver, you will be instructed on how to submit product reporting information.

D. Confidentiality of Reporting Information

Section 503B(b)(1)(B)(i) provides that outsourcing facility registrations are available for inspection to any person so requesting.

Section 503B(b)(2)(C) specifies that product reports are exempt from inspection under section 503B(b)(1)(B)(i) unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health. FDA finds that exempting from disclosure some of the information submitted in product reports would be inconsistent with the protection of the public health, specifically, for each marketed product: the name of the outsourcing facility, address of the outsourcing facility, name of the active ingredient, strength of the active ingredient per unit, dosage form, package description, and NDC of the final product (if assigned). This information is generally required on product labels or publicly available, but publication of this information will facilitate product recalls when they are necessary, and assist the public in finding outsourcing facilities that have compounded certain drug products, particularly drugs in shortage. FDA intends to publish this information on our Web site. FDA does not intend to publish information about a drug submitted in a product report if an outsourcing facility notes in the report that it has not distributed the drug and has not advised any person of its intent or ability to compound the drug.